Original Research Paper

Volume - 12 | Issue - 12 | December - 2022 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Medicine

IMPACT OF POST BOOSTER DOSE VACCINATION OF SARS Cov-2 (COVISHIELD). (A BRIEF ANNOTATION ON ANTIBODY RESPONSES IN SEROPOSITIVE PERSONS)

Dr. S.H.Talib*	Professor Emeritus, Medicine Dept. of Medicine, MGM medical college and hospital Aurangabad*Corresponding Author
Dr.Manjiri Naik	Professor and Head, Medicine Dept. of Medicine, MGM medical college and hospital Aurangabad
Dr. Awani Paithankar	Resident in Medicine Dept. of Medicine, MGM medical college and hospital Aurangabad
Dr.Abdulla Ibji	Resident in Medicine Dept. of Medicine, MGM medical college and hospital Aurangabad

ABSTRACT Introduction: Several variants of Covid-19 have also emerged especially Delta variant (B1.617.2), which have variable resistance to neutralizing antibodies, despite patient receiving vaccination. Vaccination against Covid-19 demonstrated to confer significant protection, but also has been noted to have temporal decay in antibody titre over time in various studies. Objective: To analyse and study the cases developing reinfection with COVID-19 with IgG quantitative titre in poste booster status. And to record IgG titres in healthy individuals post booster status. Material and methods: This observational study was conducted MGM Hospital, Aurangabad Maharashtra between the period of January 2022 to June 2022 on total of 32 participants. Individuals who have received 3rd dose of covid vaccination and previously with or without history of SARS COV-19 disease were included in the study.IgG titres were measured in these individuals. Two groups were made. Group A included cases with previous history of COVID-19 infection. Group B included cases with no prior history of COVID-19 infection. Results: Fatigue ,Fever ,Cough, Headache, Sore throat, Loss of smell were common symptoms in both the groups. There were 3 cases having hypertension and 2 cases with IHD in previous covid negative group. the mean values of IgG was found to be statistically significant. (p value=0.00023).Conclusion: The results have shown post booster low titres where persons are either healthy or had covid reinfection. Persons having high titres also developed reinfection. The protective cut-off value for IgG is unknown.Keywords:COVID-19 infection, IgG titre, Covid vaccine,reinfection. **BACKGROUND:** The efficacy of 3rd dose of COVID 19 vaccine, Covishield in preventing symptoms of SARS COV19 infections in persons with or without previous SARS CoV-2 disease (Healthy individuals) are reported to have variable outcome. What response would be to the 3rd jab in previously covid afflicted persons is not yet clear.

KEYWORDS :

INTRODUCTION:

Covid-19 pandemic started in March 2019. Since then, protection against Covid-19 has been most important aspect in Indian healthcare system. Vaccines were considered the most promising intervention to end the pandemic and to boost the herd immunity. A steady decline in cases, hospitalization and deaths, particularly among individuals who are at high risk of severe infection and complications were observed. Vaccination against Covid-19 demonstrated to confer significant protection, but also has been noted to have temporal decay in antibody titre over time in various studies.

Several variants of Covid-19 have also emerged especially Delta variant (B1.617.2), which have variable resistance to neutralizing antibodies, despite patient receiving vaccination. This observation raised an argument that the vaccination so provided had the protection against newer variant and otherwise. Some variants developed resistance to antibodies elicited by vaccines. Though it prevents the symptomatic outcome, but data regarding antibodies and immunogenicity of vaccine post booster dose are not yet defined.

After providing two doses of vaccination, the antibody titre decay over next 3-4 months. Vaccine effectiveness across the country is difficult since different variants have been circulating. Immunity due to vaccine and natural infection gets affected by population behaviour and public health policies tremendously. Neutralising antibody titres also decreases over a short period for both m-RNA vaccine and viral vector vaccine.

Data on immunogenicity of booster dose with Covishield is not yet meagre. Here we are going to study viral vector vaccine – ChAdOx1-nCOV-19 (Covishield vaccine). Although adverse effects were not observed at the injection site or post vaccination, however cases are reported of COVID-19 RTPCR positivity in persons with post booster vaccination. Attempt is here done to analyse and record previously RTPCR positive cases in post vaccination subjects for their immunogenicity besides healthy individuals receiving booster dose of covid 19 vaccine (without previous corona disease).

Inclusion criteria :

- Individuals who have received 3rd dose of covid vaccination and previously with or without history of SARS COV-19 disease.
- Individuals who are with comorbidities like Diabetes mellitus , Ischemic heart disease and Hypertension are included.

Exclusion criteria :

- Individuals who have not received 3rd dose of covid vaccination
- Pregnancy
- Immunocompromised individuals .

AIM

To study the antibody response after 3-6 weeks in subjects post booster dose with COVISHIELD vaccine.

OBJECTIVES:

1. To analyse and study the cases developing reinfection with COVID-19 with IgG quantitative titre in poste booster status.
2. To record IgG titres in healthy individuals post booster status.

MATERIAL AND METHODS:

The present observational study was conducted MGM Hospital, Aurangabad Maharashtra between the period of January 2022 to June 2022.The permission from Institutional ethics committee was duly obtained.

The study subjects divided into two groups A and B.

1. GROUP A: Post booster vaccinees with previous COVID 19 infection. n=16

2. GROUP B: Post booster vaccinees who were unaffected earlier with COVID-19 illness. n = 16

Method used for serum IgG COVID 19 titre was Chemiluminescent Immunoassay technique with Beckman coulter immunoassay system. A 20 micro/L serum sample is used for this quantitative technique. Analytical Range defined is between 2 to 450 AU/mL . Sensitivity being 2 AU/mL (lower limit of quantification) and 450 AU/ml being higher limit. Reports were considered positive when titre was more than 10 AU/mL . Clinical specificity of technique is 99.9%.

Statistical Analysis:
Data is entered in Microsoft Excel and was used for analysis using SPSS version 24. Mean and SD was be calculated for non modifiable variables and proportions were calculated for modifiable variables. Chi-square test will be applied for quantitative data. p- value of < 0.05 was considered statistically significant.

Table 1.Age and Gender wise distribution of both groups

Sex		Group		Total	p value
		Previous Covid Positive n(%)	Previous Covid Negative n(%)		
	Female	5(31.20)	5(31.20)	10(31.20)	0.68
	Male	11(68.80)	11(68.80)	22(68.80)	
Total		16(100)	16(100)	16(100)	
Mean Age		26.88±5.9	34.75±13.3	30.81±10.89	0.74

RESULTS:
Table 1 shows majority subjects are 11(68.80%), being males in both the groups. Mean age in Covid Positive group was 26.88±5.9 years and 34.75±13.3 years in Covid Negative group. The difference noted was insignificant

Table 2. Blood Group wise distribution of both groups

Blood group	Previous Covid Positive n(%)	Previous Covid Negative n(%)	Total
A Rh -ve	02(12.5%)	01(6.3%)	03(9.4%)
A Rh +ve	02(12.5%)	0(0.0%)	02(6.3%)
AB Rh +ve	01(6.3%)	03(18.8%)	04(12.5%)
AB Rh-ve	0(0.0%)	01(6.3%)	01(3.1%)
B Rh -ve	02(12.5%)	00(0.0%)	02(6.3%)
B Rh +ve	0(0.0%)	01(6.3%)	01(3.1%)
B Rh+ve	05(31.3%)	01(6.3%)	06(18.8%)
O Rh +ve	03(18.8%)	08(50.0%)	11(34.4%)
O Rh-ve	01(6.3%)	01(6.3%)	02(6.3%)

Table 2 shows majority subjects in covid positive group 5(31.3%) had B Rh+ve blood group followed by 3(18.8%) O Rh +ve blood group. While subjects in covid negative group, 8(50.0%) had O Rh +ve blood group followed by 3(18.8%) having AB Rh +ve blood group.

Table 3 Distribution of study subjects according to symptomatology

Symptoms	Previous Covid Positive n(%)	Previous Covid Negative n(%)	Total
Cough	09(56.25%)	05(31.25%)	14(43.70%)
Nasal discharge	2(12.5%)	01(6.25%)	03(9.40%)
Headache	09(56.25%)	05(31.25%)	14(43.70%)
Sore throat	10(62.50%)	07(43.80%)	17(53.10%)
Loss of smell	08(50.00%)	01(6.25%)	09(28.10%)
Diarrhoea	01(6.25%)	01(6.25%)	02(6.30%)
Fever	10(62.50%)	08(50.00%)	18(56.30%)
Breathlessness	0(0.00%)	01(6.25%)	01(3.10%)
Fatigue	14(87.50%)	09(56.25%)	23(71.88%)

Table 3 shows Fatigue ,Fever ,Cough, Headache, Sore throat, Loss of smell were common symptoms in both the groups.

Table 4 Distribution of study subjects according to comorbidities present

Comorbidities	Previous Covid Positive n(%)	Previous Covid Negative n(%)	Total
Hypertension	0(0.00%)	03(18.08%)	03(9.40%)
Diabetes Mellitus	0(0.00%)	01(6.25%)	01(3.10%)
IHD	0(0.00%)	02(12.50%)	02(6.30%)

Table 4 shows no comorbidities were seen in previous covid positive group. There were 3 cases having hypertension and 2 cases with IHD in previous covid negative group.

Table 5 Comparison of mean serum IgG titres values in both groups

IgG titre	Group	N	Mean	Std. Deviation	Std. Error of Mean	T test p value
	Previous Covid Positive	16	98.5644 ± 77.6455	38.82279	9.70570	0.00023
	Previous Covid Negative	16	18.7288 ± 6.20238	3.10119	7.52530	

Table 6 shows after applying unpaired t test, the mean values of IgG was found to be statistically significant.

(p value=0.00023)

Table 6 Comparison of high and low titres in both groups

	High titre	Low titre
Previously covid positive	1	15
Previously covid negative	6	10

Table 6 shows distribution of cases as those with high titre vs those with low titres in both groups. The difference was found to be statistically significant with p-value of 0.032509

DISCUSSION :
It is well known cited observation that persistence of immunity beyond six months post covid 19 vaccinations failed to recognise and assess new onset of covid 19, as patients having high titre had also developed subsequent covid 19 disease. A higher number of cases also revealed in earlier studies about low IgG titre of candidates who do not develop covid 19 disease. It is unclear whether natural immunity post infection gets suppressed by vaccine immunogenicity. It is also unclear that the breakthrough infection is due to new emergent variants unprotected by vaccine, besides ? suppressed natural immunity post infection.

The validity and utility of vaccine is still unknown as the data keeps on changing, following recedance or weaning of immunity over time with occurrence of new variants. The much concerns about vaccine efficacy has evolved with occurrence of delta variant which was associated with higher viral load and transmissibility. Modern vaccines have shown decrease response of neutralizing antibodies to delta variant.

Israel first used the vaccine to respond to delta wave with booster programme followed by India, allowing people above 60yrs of age and medical professionals to receive the 3rd dose. Administration of booster dose with interval 3 week was associated with significant reduction of infection and severe covid 19 Little known about how long the reported increase in immunity with booster dose would last with effective protection with B and T cell response on long term observation.

Providing booster dose posed many ethical issues when Israel and India used these doses, when only less than 5% of Africa's population were fully vaccinated and unvaccinated people develop infection and transmitted this infection globally. These people and the countries contributed to the development of new variants with high potential transmissibility. Nevertheless, booster dose is required for keeping high B and T cell immunity for greater length of time. Therefore, booster dose is considered a fruitful option negotiating the problems. The present study is based to assess IgG titre in post booster status.

The decrease in immunity has been confirmed in , several observational studies reporting a decrease in effectiveness against infection 5-6 months after 2nd dose . Although this decrease was less pronounced for severe form of disease or hospitalized patients. These observations have created a questionable mark of timing and efficacy of third dose/ booster dose . There are many supportive data's and concordant analysis showed that 3rd dose was useful in enduring a boost in humoral response especially patients of cancers , on steroids or on immunosuppression.

When second wave of COVID-19 become pandemic and touched

Indian shores, many Indians among us were gasping of oxygen for fight against deadly virus. No sooner we developed a weapon against this COVID-19 with development of vaccination .A promising ray of hope to combat this deadly problem and saving normal lives, India approved mainly 3 COVID-19 vaccination viz: COVISHIELD, COVAXIN and SPUTNIK. All three vaccines have proven efficacy against corona virus. Once virus gains an access to target cell , the host immunity system recognizes the virus or its surface epitome/vaccine eliciting the innate or adaptive immune response.

Gresiya waltron et-al (2021) suggested that COVID -19 neutralizing antibodies predict disease severity and survival. Further vaccine trial by HO, M-S et-al (2005) suggested in their vaccine trial, the antibody response, SARS severity, high levels of neutralizing antibodies in vaccinees that predicted the reduced risk of ICU admission, severe illness and death. It is therefore mandatory to monitor neutralizing antibodies.

In COVID-19 what is overall neutralizing antibodies response in the individuals besides RBD specific neutralizing antibodies is not yet clarified therefore the situations of this kind other targeting antibodies needed to get studied. Vaccine IgG antibodies production perhaps provide information on limited reference for immune status. Positive results for neutralizing antibodies post vaccination does not confirm absolute protection and negative results does not necessarily indicate non protection.

In our study , 32 cases who received booster dose of vaccine timely placed after 6 months after 2nd dose revealed variable results of IgG titres i.e. 7 cases showed high titres while 25 cases has shown low titres. The mean values of IgG was found to be statistically significant (p value=0.00023) (table no 5) The non modifiable factors were statistically insignificant (table no 1)

We agree vaccine immunoglobulin production merely provide limited information on immune status. The observation helps in understanding for advising supplementary vaccination and timed interval that may strengthen the immune domain. In our study all cases of IgG antibody titre was carried out after 3rd dose of vaccine. Certain observation here need attention whether the vaccine is fruitful or less protective in elderly than younger. The protection Cut-off value for IgG considered as safe is not yet defined. It is also known that the titres of neutralization antibody were positively correlated with plasma CRP and inversely related to lymphocyte count at the time of admission.

This observation further requires strengthening, whether IgG levels, CRP and lymphocyte count are helpful in deciding the need for booster dose.

One also be uprise of the fact that, continued fluctuation of epidemic is closely related to the mutation of viruses. Variety of mutants are evolved namely alpha beta gamma delta. Emergence of variants of SARS COV-2 B117 in UK and delta-135-1 of South Africa aroused concern worldwide. Presently we have no understanding with observed values in study whether these variants have escaped immunity resulting from previous infection or vaccination.

There is also need to study on neutralizing antibodies on large scale regarding susceptibility to these variants We further have no concrete reports whether previous infection with certain strains of corona could protect individuals against future strains. The subject of cross reactivity of neutralizing antibodies is ill understood yet.

CONCLUSION:

There was remarkable difference in post booster IgG antibody titres of IgG in persons who were either COVID positive or negative; the mean values of serum IgG was found to be statistically significant (p value=0.00023). The limitation of this study is the small sample size. The results have shown post booster low titres where persons are either healthy or had covid reinfection. Persons having high titres also developed reinfection. The protective cut-off value for IgG is unknown.

We need to understand whether previous infection with certain strains of corona protect infection against variety of mutant. Large scale timely placed booster doses of vaccine with neutralizing antibodies and their correlation with plasma CRP, lymphocyte count are further needed for better understanding of immune scenario.

REFERENCES:

1. Zeng G, Wu Q, Pan H, Li M, Yang J, Wang L, Wu Z, Jiang D, Deng X, Chu K, Zheng W, Wang L, Lu W, Han B, Zhao Y, Zhu F, Yu H, Yin W. Immunogenicity and safety of a third dose of CoronaVac, and immune persistence of a two-dose schedule, in healthy adults: interim results from two single-centre, double-blind, randomised, placebo-controlled phase 2 clinical trials. Lancet Infect Dis. 2022 Apr;22(4):483-495.
2. Yue L, Zhou J, Zhou Y, Yang X, Xie T, Yang M, Zhao H, Zhao Y, Yang T, Li H, Xiang H. Antibody response elicited by a third boost dose of inactivated SARS-CoV-2 vaccine can neutralize SARS-CoV-2 variants of concern. Emerging Microbes & Infections. 2021 Jan 1;10(1):2125-7.
3. Skrzat-Klapaczyńska A, Bieńkowski C, Kowalska J, Paciorek M, Puła J, Krogulec D, Stengiel J, Pawełczyk A, Perlejewski K, Osuch S, Radkowski M. The Beneficial Effect of the COVID-19 Vaccine Booster Dose among Healthcare Workers in an Infectious Diseases Center. Vaccines. 2022 Apr 2;10(4):552
4. Arbel R, Hammerman A, Sergienko R, Friger M, Peretz A, Netzer D, Yaron S. BNT162b2 vaccine booster and mortality due to Covid-19. New England Journal of Medicine. 2021 Dec 23;385(26):2413-20.
5. Vadrevu KM, Ganneru B, Reddy S, Jogdand H, Raju D, Sapkal G, Yadav P, Reddy P, Verma S, Singh C, Redkar SV. Persistence of immunity and impact of third dose of inactivated COVID-19 vaccine against emerging variants. Scientific reports. 2022 Jul;12(1):12038-.
6. Barda N, Dagan N, Cohen C, Hernán MA, Lipsitch M, Kohane IS, Reis BY, Balicer RD. Effectiveness of a third dose of the BNT162b2 mRNA COVID-19 vaccine for preventing severe outcomes in Israel: an observational study. The Lancet. 2021 Dec 4;398(10316):2093-100.
7. Iketani S, Liu L, Nair MS, Mohri H, Wang M, Huang Y, Ho DD. A third COVID-19 vaccine shot markedly boosts neutralizing antibody potency and breadth. MedRxiv. 2021 Jan 1.
8. Moreira Jr ED, Kitchin N, Xu X, Dychter SS, Lockhart S, Gurtman A, Perez JL, Zerbini C, Dever ME, Jennings TW, Brandon DM. Safety and efficacy of a third dose of BNT162b2 COVID-19 vaccine. New England Journal of Medicine. 2022 May 19;386(20):1910-21.