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ORIGINAL ARTICLE

Sinopharm and Sinovac COVID-19 vaccines; Prevalence and risk factors for post full vaccination weak immunity.

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ABSTRACT… Objective: To see the prevalence and risk factors for post full vaccination (Sinopharm and Sinovac COVID-19 vaccines) weak immunity in persons with no history of viral exposure. **Study Design:** Prospective Observational. **Setting:** Syed Research Centre, Sialkot. **Period:** Nov 2021 to Feb 2022. **Material & Methods:** Eighty two individuals (male/female, aged: 24-70 years) were enrolled from District Sialkot (Pakistan). Two doses of Sinopharm or Sinovac COVID-19 vaccine were administered to each participant before blood sampling. The quantity of COVID-19 spike immunoglobulin G against SARS-CoV-2 (5-Antigen) was detected in serum using chemiluminescence immunoassay technique [threshold titer: 7.1 (detection), 105. 63 (seroprotection), 492.96 BAU/mL (strong humoral response)]. **Results:** Overall, 96.3% seropositivity, 89% seroprotection, and 37.8% (n = 31) weak immune response were recorded. Whereas, mean antibody titer was found to be 2312.02 (range: 0.0 – 28711.74) BAU/mL. A vaccinated male had approximately 4 folds (95%CI: 1.297 – 11.504; p = .002) more likelihood of weak immune response than females. Similarly, the rate of poor immunological outcome was higher in individuals with >24.9 Kg/m^2 (69.2%, n = 27) body mass index compared to ≤24.9 Kg/m^2. A person with Sinopharm COVID-19 vaccine was more vulnerable to weak immune response than Sinovac vaccinated participants (RR = 2.351; 95%CI = 1.327 – 4.167; p .002; 57.6% vs. 24.5%, respectively). Co-occurrence of age (>47 years) and BMI (>24.9 Kg/m^2) existed in 11 of 28 males (39.3%) with impaired immunogenicity. **Conclusion:** The high rate of post full vaccination weak immune response is alarming. Gender, BMI, and vaccine type were amongst the predictors for diminished humoral response.

Key words: Body Mass Index, COVID-19 Vaccines, Immunoglobulin G, Prevalence, Risk Factors.

INTRODUCTION

Vaccination against SARS-CoV-2 virus of COVID-19 pandemic is a generally-accepted practice in the world despite of vaccine hesitancy. Luckily in Pakistan, the vaccine coverage of full vaccination hit a satisfactory figure of 43.5% beside booster dosage on emergence of Omicron variant.[1,2] The credit of this accomplishment majorly goes to public medical health facilities[3] and other societal segments e.g. educational institutes.

Production of sufficient amount of immunoglobulin G (IgG) in the blood serum on administration of effective COVID-19 vaccine usually makes a person safe[4] from the viral infection. Its importance increases manyfold when other preventive measures e.g. social distancing are least observed. Recently reported Omicron mutant is milder than its predecessors in terms of compulsory hospitalization; and can be addressed with the routinely used vaccines in the field.[5,6] Two inactivated virus-based vaccines i.e. Sinopharm COVID-19 and Sinovac COVID-19 vaccine are very useful in this context. The vaccines elicit antibody G by mounting B and T cells which ultimately neutralize the receptor binding domain of S protein in the virus.[6,7] Moreover, the immune response persists for a long time.

The serologists have set detection and protection values of antibody titer on full vaccination for reference. Whereas, the titer less than 492.96

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BAU/mL [70 AU/mL] is referred as weak immunogenecity.[8,9] The weak humoral response puts an individual in the zone of high susceptibility to viral infection; hence, necessitates booster dosage to manage the deficiency. The weak immunity can be associated with certain characteristics[10] e.g. body mass index or dose interval of any vaccine.

There is no evidence of research papers on weak immune response after administration of COVID-19 vaccine (Sinopharm or Sinovac) particularly with reference to Sialkot (Pakistan). Present work was designed to address the gap with the objective to see the weak immunological response on full vaccination by the two vaccines at Sialkot beside its potential predictors. The outcomes will help the concerned authorities to consider the predictors before any COVID-19 vaccination public drive.

MATERIAL & METHODS

The present prospective observational study was conducted between Nov 2021 and Feb 2022 at District Sialkot (Pakistan) after obtaining permission from the ethics committee of Syed Research Center, Sialkot. The residents of the District are health conscious and medical research friendly.

Ninety six i.e. 80 (sample size) plus 16 (nonresponse risk @ 10%) were registered from four administrative subdivisions natively called Tehsils (@ 24 per Tehsil) of Distt. Sialkot using purposive sampling technique. All the male/female (aged: 18-70 years) participants self-reporting no history of infection from Corona virus or pre-vaccination IgG detection in serum were included. However, all those who had any autoimmune disorder, chronic disease, chemotherapy, pregnant/breastfeeding women, and/or been vaccinated with vaccine other than Sinopharm/Sinovac COVID-19 were excluded. Moreover, study participation consent of the recruiters was mandatory.

To each participant, two doses of vaccine were administered at prescribed dose interval along with recording of sociodemographic and clinical information. After 28 days of 2nd dose, the blood was sampled through phlebotomy procedure for IgG titer. The titer was estimated using SARS CoV IgG II Quant Assay (Abbott Diagnostics) also known as chemiluminescence immunoassay technique. The technique was approved by FDA on the basis of robust evidences of concordance (94.4%) between the test at threshold of 7.1 BAU/mL [1BAU = 0.142 AU] and the Plaque Reduction Neutralization Test 90% at 1:40 ratio. Cut-off titer of 105.63 BAU/mL was assumed to discriminate responders to vaccination with a protective titer.[11] Furthermore, a titer of 492.96 BAU/mL[12] was taken as threshold for strong immune response; upper limit: 285,714.28 BAU/mL.

The Mann Whitney U test was applied to compare mean antibody G titer using data in binomial variables. Similarly, potential predictors for weak immune response were recorded on processing the data in 2x2 cross tabulation technique and chi-square test. For the tests, a p value ≤ 0.05 was considered statistically significant. The techniques in SPSS version 25 (IBM Corp., Armonk, NY) were used for the purposes.

RESULTS

Of ninety six subjects, 82 (85.4%) adhered with the prescribed COVID-19 vaccine's dosing regimen and blood testing for IgG titer; hence, recruited for final titer assessment and statistical analyses. The seroprotection rate of 89% (n = 73) was found on quantification of IgG through immunoassay [threshold value = 105.63 BAU/mL]. Whereas, the seropositivity rate approached to 96.3%, n = 79 taking ≥7.1 BAU/mL value as a reference for positive results. All the three seronegative cases showed no immunological response. The rate of demographic characteristics included: 70.7% (male), 48.7% (normal body mass index), and 81.7% (no history of hypertension and/or diabetes). Moreover, biological age ranged between 24 and 70 years.

Concentration of IgG in the blood sera of males was significantly lower than that of the females (U = 294.000, p = .000) using Mann Whiteny U test as shown in Table-I. Similarly, there was low concentration in the subjects with obese/higher

class of BMI in comparison to normal BMI (Mean Rank 27.63 vs. 54.08, respectively). On the other hand, there was significant difference between the Ranks against Sinopharm (29.98) and vaccine (49.26) for non-normal distribution of antibody titer (p = .000). Similarly, lower concentration was seen for time interval of ≤35 days between 2nd dose of vaccine and blood sampling than > 35 days.

The elicited immunological response on full vaccination using Sinopharm or Sinovac COVID-19 vaccine was revealed, as: 2312.02± 4856.7; range 0.0 – 28711.7 BAU/mL. Moreover, diminished response (i.e. less than 492.96 BAU/mL; threshold value) was recorded in 31 (37.8%) participants. Table-II indicates prediction of a particular feature of a variable towards weak immune response using 2x2 crosstabulation and chi-square test of association. A vaccinated male had approximately 4 folds (95%CI: 1.297 – 11.504; p = .002) likelihood of weak immune response than females. Similarly, the rate of such poor immunogenicity was higher in individuals with >24.9 Kg/m^2 (69.2%, n = 27) compared to ≤24.9 Kg/m^2. Surprisingly, more frequent weak response was seen in the side of individuals free from comorbidity than comorbid of hypertension and/or diabetes. A person with Sinopharm COVID-19 vaccine was more susceptible to weak immune response than Sinovac vaccinated participants (RR = 2.351; 95%CI = 1.327 – 4.167; p .002; 57.6% vs. 24.5%, respectively).

Weak immune response was noticed in 2 females (66.67% of total 3) and 11 males (39.3% of total 28) having demographic characteristics, as: Aged >47 years and BMI >24.9 Kg/m^{2}as displayed in the Figure-1. Similarly, higher BMI also contributed in another set of male participants where the rate of weak immunological response was recorded to be 50% (n = 14).

Variable	Mean Rank of Titer	Mann Whitney U	P****
Gender* Male Female	 34.57 58.25	294.000	.000
Age (years) ≤ 47 > 47	 43.28 39.72	767.500	.498
BMI (Kg/m^2) ≤24.9 >24.9	 54.08 27.63	297.500	.000
Comorbidity** No Yes	 40.77 44.77	453.000	.557
Vaccine (COVID-19) Sinopharm Sinovac	 29.98 49.26	428.500	.000
Vaccine's dose interval (days) ≤ 35 > 35	 47.60 39.53	498.000	.188
Interval between 2nd dose and blood sampling (days)*** ≤ 35 > 35	 34.16 50.85	490.000	.002

Table-I. Comparative antibody titer after 2nd dose of COVID-1 vaccines
***no case of transgenders; **hypertension and/ diabetes; ***sampling for IgG titer; ****asymmetric sig. (2-tailed)**

Variable	Rate of Weak Immune Response; % (n)	RR; 95%CI	p
Gender* Male Female	 48.3 (28) 12.5 (3)	3.862; 1.297 – 11.504	.002
Age (years) ≤ 47 > 47	 36.6 (15) 39.0 (16)	.938; .538 – 1.634	.821
BMI (Kg/m^2) ≤24.9 >24.9	 9.3 (4) 69.2 (27)	7.442; 2.860 – 19.368	.000
Comorbidity** No Yes	 43.3 (29) 13.3 (2)	1.528; 1.145 – 2.039	.031
Vaccine (COVID-19) Sinopharm Sinovac	 57.6 (19) 24.5 (12)	2.351; 1.327 – 4.167	.002
Vaccine's dose interval (days) ≤ 35 > 35	 37.1 (23) 40 (8)	1.078; .576 – 2.019	.816
Interval between 2nd dose and blood sampling (days)*** ≤ 35 > 35	 27.8 (10) 45.7 (21)	1.643; .890 – 3.036	.098

Table-II. Predictors for weak immune response in fully vaccinated individuals (N = 82)

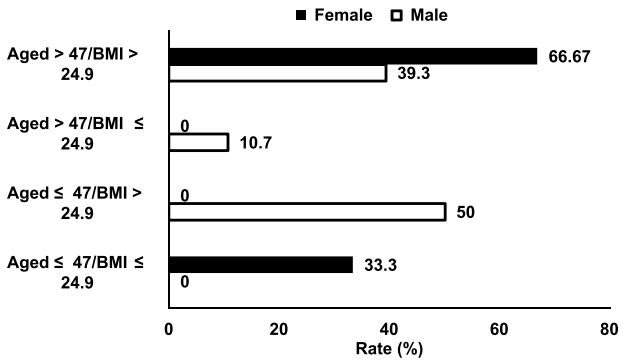

Figure-1. Rate of weak immune response in sexes with regard to age and BMI

Population (male = 28, female = 3); Weak immune response (IgG titer less than 492.96 BAU/mL in fully vaccinated individuals by Sinopharm or Sinovac COVID-19 vaccine); Age (years), BMI (Kg/m^2)

DISCUSSION

The nonadherence of initially registered 14 participants with dosing regimen and blood sampling for the IgG estimation indicates poor vaccine acceptancy on somewhat half-hearted willingness[13] and/or vaccine hesitancy to participate in the study.[4,13,14] The seroprotection rate (89%) marks high effectiveness-cum-safety of the COVID-19 vaccines. It is even higher than 75%[15] for a under trial vaccine; hence, proposes human safety from the infection. However in contrast to previous literature[9,10], recording of three healthy cases with no seroconversion is a matter of concern. Such a deficiency is usually expected from immunocompromised/multiple sclerosis patients with impaired B cells mounting.[12,16]

Compared to females, diminished virus-neutralizing antibody production in males is in the line with a previous study highlighting suppressive impacts of testosterone on post-vaccination IgG against Omicron variant; so, it is based on hormonal differentiation.[5,6,7,10,17] Greater than normal BMI hampers the vaccination-elicited response[10,18] through intrinsic immunological perturbations. Similarly, the weaker immunogenicity from Sinopharm COVID-19

vaccine than Sinovac COVID-19 vaccine seems to be multifactorial determinants e.g. antirheumatic therapy[19] and/or genetic makeup.

There is waning of immunogenicity with passage of time; hence, deserves booster dose[20] of the vaccine. The finding of comparatively higher rate of weak immune response in the blood samples of more than 35 days is in the line of this time-based decline in COVID-19 vaccine-mediated immunity. Insignificant difference between the rate of weak immunity rate of on time vaccination or delayed vaccination is a sharp contradiction to a previously reported data[21] emphasizing better immune response in the delayed cases. In the findings of present work, no difference in rate of weak response between younger and older groups is opposite to the general concepts of the immunologists that mounting of B and T cells becomes weak and nondurable in the older age groups of human population.[10,11,17,22]

Obesity/overweight[18,23] accompanied by older age of the vaccinated individuals results in immune response with low antibody profile. It is also independent of gender. Moreover, it is also expected that mere obesity can lead to decline in IgG production via suppressive mechanism especially with reference to Omicron mutant.[24,25]

The data of the study restricts to small sample size i.e. 96 subjects due to limited human and financial resources. Exclusion of pregnant/breastfeeding women seems to make the study a little bit biased. Similarly, self-reporting of no previous history of viral exposure may carry misinformation from the participant side.

CONCLUSION

The rate of seroprotection was found 2nd to seropositivity after full vaccination i.e. two doses of Sinopharm or Sinovac COVID-19 vaccine on Internationally approved time intervals. Simultaneously, the weak immune response was also prevalent. Maleness, BMI (higher than normal), or Sinopharm COVID-19 vaccine were amongst the predictors for the weak production of the antibody titer. Similarly, impaired immunogenicity showed association with co-occurrence of higher age group and abnormal BMI i.e. higher than normal.

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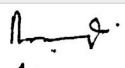
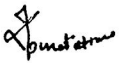
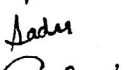
1	Sahibzada Syed Masood us Syed	Design of study, Overall script.	
2	Abid Ali Ranjha	Lab work.	
3	Sidra Ghazanfer	Lab work.	
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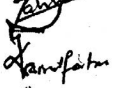
5	Syeda Zahra Najam	Data collection.	
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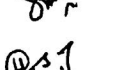
7	Hassan Osman Muhmood	Data collection.	
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