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COVID-19 anti immunoglobulin G antibodies serum levels among health care workers post COVID -19 vaccination: A single center study

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Abstract

Coronavirus disease 2019 (COVID-19) pandemic has urged the scientific community internationally to find answers in terms of therapeutics and vaccines to control the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The post vaccination immune response differs between individuals especially health care workers who are the first line of defense to combat this disease. Our aim was to measure levels of anti-IgG antibodies titer post COVID-19 vaccination among health care workers in Suez Canal University Hospital. The study included 141 healthcare workers. Of these, 54 were physicians, 80 nurses, 6 health service workers, and one security guard. We used the Roche Elecsys Anti-SARS-CoV-2 assay for serological detection of IgG. Seropositive was found in 96.5% of the participants, and 43.3% of them had evidence of the prior history of COVID-19 infection. The highest titers of IgG in sera were found in the youngest age groups (20 – <35) years with a mean of 335.1 U/ml. Participants who received the Sinovac vaccine had the highest mean IgG titer, 354.6U/ml; followed by Sinopharm (mean 352.15 U/ml) then Pfizer and Moderna (311.7U/ml) and AstraZeneca vaccine had the least mean level (267.31U/ml). Fatigue was the most significant short side effect occurring with 34% of the participants. In conclusion, there was a significant rising in serum IgG titer post-vaccine, and better antibody response in those previously infected with COVID-19. The post-COVID-19 vaccine serum IgG titers were affected by age, prior history of COVID-19 infection, and type of vaccine while short side effects post-vaccination may be affected by age and type of the vaccine.

Keywords: Coronavirus, Covid-19, Covid-19 vaccine, IgG antibody response.

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Introduction

Coronavirus disease 2019 (COVID-19), a highly infectious viral infection produced by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has had a disastrous effect on the world's demography, resulting in more than 6

million deaths globally as of March 2022.[1] SARS-CoV-2 quickly spread throughout the world after the first instances of this predominantly respiratory viral illness were discovered in late December 2019 in Wuhan, China, causing the World Health Organization (WHO) to proclaim it a worldwide pandemic on March 11, 2020.[1] Egypt is one of the five African countries reporting the highest number of cases. Egypt had more than 42,000 cases and 1,672 deaths as of 15 June 2020 (3.6% case fatality rate).[2]

Soon after, many vaccines were discovered, and various governments began large immunization efforts.[3] The development of an efficient immunity and antibody response against SARS-CoV2 was the common objective of all COVID-19 vaccines, even though their techniques of design varied. The post-vaccination immunological response and antibody levels, however, may vary from person to person.[4]

Although available commercial serological assays do not provide information on whether SARS-CoV-2 antibodies confer immune protection, recent reports using specialized laboratory-based neutralization assays have observed a marked correlation between the levels of SARS-CoV-2 spike/receptor binding domain (RBD) antibodies and the neutralization capacity of patient sera, suggesting its potential beneficial role in clearance.[5]

Since vaccination effectiveness can vary depending on the vaccine type, patient characteristics, and SARS-CoV-2 variations, it is important to assess vaccine effectiveness objectively. These vaccines were developed using different technologies.[6] The vaccination for COVID-19 was recommended by health agencies including WHO for the limitation of the COVID-19 pandemic by forming active acquired immunity resulting in reduced symptomatic patients' number and interrupting transmission of the virus.[7]

By triggering immune responses against SARS-CoV-2, these vaccines can provide protection from the pathophysiology and clinical symptoms of COVID-19. Serum IgG antibodies, which represent humoral immune responses, and vaccine-specific effector T cells, which represent cellular immunological responses, make up the majority of immune reactions detected post-vaccination. Despite the lack of a defined level to correlate with protection, IgG antibodies were generated at high levels following COVID-19 vaccinations.[8]

Due to their frequent and prolonged professional contact with patients and exposure to the SARS-CoV-2 virus, healthcare workers (HCWs) are more likely to contract COVID-19 and become infected. During the period from January 2020 to May 2021, between 80,000 and 180,000 HCWs perished from COVID-19, according to WHO data. HCWs are seven times more likely to contract COVID-19 than other employers.[9] The necessity of immunizing healthcare professionals cannot be overstated. They are essential in educating the public about the value of vaccination, and as immunized HCWs may have relief from specific symptoms and severe illness, they lessen the risk of infection transfer to patients.[9]

There are 9 vaccines approved to be used in Egypt which included: Moderna (Spikevax) vaccine, Pfizer/BioNTech (Comirnaty) vaccine, Gamaleya (Sputnik Light), Gamaleya (Sputnik V), Janssen (Johnson & Johnson), Sinopharm (Beijing), Oxford/AstraZeneca (Vaxzevria), Serum Institute of India Covishield (Oxford/ AstraZeneca formulation) and Sinovac (CoronaVac). Five of them were included in our study (Moderna, Pfizer/BioNTech, Oxford/AstraZeneca, Sinovac and Sinopharm vaccines).[10]

These vaccines were developed using different technologies. The Pfizer/BioNTech BNT162b2 and Moderna mRNA 1273 COVID-19 vaccines are messenger RNA (mRNA)-based vaccines, which encode SARS-CoV-2 prefusion-stabilized full-length spike protein, with efficacy rates of 95% and 94.1%, respectively. Likewise, the vaccines developed by Oxford/AstraZeneca and Johnson and Johnson are considered viral vector-based vaccines. The Oxford/AstraZeneca vaccine consists of a replication-deficient chimpanzee adenoviral vector ChAdOx1 containing the SARS-CoV-2 structural surface glycoprotein antigen (spike protein; nCoV-19) gene, with an efficacy rate of 70%. Both the Chinese vaccines (Sinopharm and Sinovac/CoronaVac) are inactivated vaccines,

which use killed SARS-CoV-2 virus. Overall, all these vaccine types met the necessary criteria for safety and efficacy as evaluated by the WHO.[10]

This study aimed to assess the human immune response post-COVID-19 vaccination, especially IgG levels among HCWs in Suez Canal University Hospital, and to detect short-term side effects post-vaccination.

Patients and Methods

The study was carried out as a cross-sectional descriptive study at Suez Canal University hospital, Ismailia, Egypt. The study population included a random sample of healthcare providers working at this hospital, started in November 2021, and ended in November 2022.

Criteria of selection

A stratified random sample of 141 HCWs participated in the survey using a staffing list as the sampling frame. Participants were chosen according to their category of health care providers. According to those who applied to receive the vaccination, the stratification was founded on the cadre of medical personnel. The staffing list was obtained from the infection control office in the hospital.

Patient assessment

All selected HCWs were subjected to a structured interview-based questionnaire consisting of the first part: individual socio-demographic characteristics and the second part included: Risk factors for COVID-19 transmission through contact with a known infected person or previous history of infection. Vaccination history was also taken including doses and duration from receiving the last dose of the vaccine.

Laboratory procedure

Venous blood samples (5 ml) were collected from all study participants aseptically in sterilized sample tubes. Before beginning the experiment, the serum was isolated and stored at - 20° C. The COVID-19 IgG titer was assessed using commercially available kits (Roche Elecsys Anti-Sars-CoV-2 S assay kits, F. Hoffmann-La Roche AG Company, Switzerland), according to the manufacturer's instructions. The assay is an electro-chemiluminescent immunoassay (ECLIA), with a sensitivity of 98.8 % and specificity of 100%.

Interpretation of the results

The analyte concentration of each sample (U/ml) was automatically determined by an automatic analyzer (Elecsys and cobas® e immunoassay analyzers, F. Hoffmann-La Roche AG Company, Switzerland). The results were interpreted according to the manufacturer's interpretation as follows: IgG titer < 0. 8 U/ml was considered negative for anti-SARS-CoV-2-S antibodies, and IgG titer ≥ 0. 8 U/ml was considered positive for anti-SARS-CoV-2-S antibodies.

Ethical considerations

The study protocol was reviewed and approved by the Research Ethics Committee of the Faculty of Medicine, Suez Canal University (reference no. 4692, dated October 2021). A written informed consent was obtained from each participant before being included in the study.

Statistical Analysis

Data were analyzed with the Statistical Package for the Social Sciences (SPSS) software (version 20.0. IBM Corporation, Armonk, New York) Numbers and percentages were used to describe qualitative data. The Kolmogorov-Smirnov test was employed to confirm the distribution's normality. Range (minimum and maximum), mean, standard deviation, median, and interquartile range (IQR) were used to characterize quantitative data. The obtained results were declared significant at the 5% level. The following tests were used: Kruskal Wallis analysis: to compare more than two examined groups using non-normally distributed quantitative variables, Chi-square analysis: To compare various groups using categorical variables, One Way ANOVA examines the means of two or more independent groups to see if there is statistical evidence that the related population means differ significantly. Chi-square test: For categorical variables, to compare different groups. The independent t-test: also called the two-sample t-test or student's t-test, is an inferential statistical test that evaluates

whether there is a statistically significant difference between the means in two unrelated groups.

Results

Demographic data are summarized in Table 1. The majority of the studied population were males (55.3%), and the mean age was 34.41 years (± 13.24). Also, the majority of the population lived in urban areas (72.3%). There were 54 doctors (38.3%), 80 nurses from different departments of the hospital (56.7%), 6 health service workers (4.3%), and one security guard. According to previous history of COVID-19 infection, study subjects were divided into two groups: those with a history of COVID-19 infection (Group A), accounted for 41.8%, while those with no history of COVID-19 (Group B) represented 59.2% as shown in Figure 1.

Table 1. The Socio-demographic data of the 141 studied subjects.

Demographic Data	No.	%
Sex		
Male	78	55.3
Female	63	44.7
Age (/years)		
20 – <35	93	66.0
35 – 50	30	21.3
>50	18	12.8
Min. – Max.	21.0 – 68.0	
Mean ± SD.	34.37 ± 13.28	
Median (IQR)	29.0 (25.0 – 40.0)	
Residence		
Rural	39	27.7
Urban	102	72.3
Occupation		
Doctor	54	38.3
Nurse	80	56.7
Worker	6	4.3
Security Guard	1	0.7

IQR: Inter quartile range SD: Standard deviation.

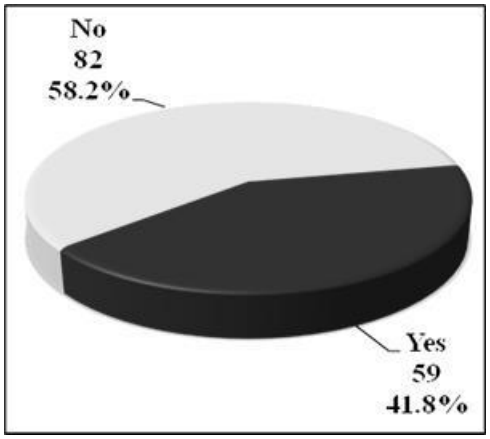

Figure 1. Pie Chart showing the distribution of the studied population regarding previous history of COVID-19 infection.

A total of 141 serum samples were collected from the HCWs received vaccines. Using a cut off value of 0.8 U/ml, according to the manufacturer's instructions, there was a significant rising of serum IgG titer post-vaccine accounting for about 96.5% of the studied samples, and 3.5% had negative values of serum IgG titer (≤ 0.4 U/ml).

Most of the studied subjects received AstraZeneca and Sinovac vaccines, Sinovac vaccination group had the highest levels (354.66±115.98) post immunization as demonstrated in Table 2.

Table 2. Distribution of the 141 studied cases according to vaccine type.

Vaccine type	No.	(%)	Serum IgG (U/mL)			*p* value
			Min. – Max.	Mean ± SD.	Median	
AstraZeneca	59	41.8	<0.4 – 511.0	267.31 (± 149.94)	297.00	0.002[1]
Sinopharm	23	16.3	<0.4 – 630.0	352.15 (± 173.34)	410.00	
Sinovac	53	37.6	21.0 – 525.0	354.66 (± 115.98)	376.00	
Pfizer and Moderna (m-RNA vaccines)	6	4.2	8.00- 451.0	311.7(± 163.1)	348.00	

[1] Chi square test Statistically significant at $p \leq 0.05$

Data in Table 3 compare detailed post-vaccine short-term side effects between the two groups. A total of 79 (56%) subjects suffered from post-vaccine complications. The most commonly reported complications were fever and generalized body ache. Generalized body ache was the most commonly occurring complication with 47.5% in Group A and 24.4% in Group B, the difference between the two groups was statistically significant (p<0.05).

Table 3. Distribution of the 141 studied cases according to post-vaccine complications according to previous history of COVID-19 infection or not.

Presence of post vaccine complications	Total (n=141)		Previous COVID-19 Infection (n= 59)		No previous COVID-19 Infection (n= 82)		*p* value
No complications	62	44.0	21	35.6	41	50	NS[1]
Fever	37	26.2	18	30.5	19	23.2	NS[2]
Skin erythema	2	1.4	1	1.7	1	1.2	NS[1]
Headache	24	17.0	11	18.6	13	15.9	NS[1]
Generalized body ache	48	34.0	28	47.5	20	24.4	0.004[2]
Cough	5	3.5	3	5.1	2	2.4	NS[1]
Dyspnea	2	1.4	0	0	2	2.4	NS[2]
Upper limb edema	1	0.7	1	1.7	0	0	NS[1]
Vomiting	1	0.7	1	1.7	0	0	
Arm weakness	2	1.4	1	1.7	1	1.2	

[1] Chi square test, [2]Fischer's Exact test. $P > 0.05$ is not significant (NS).

The mean age of the participants who reported fever was 30.86 (± 7.95), while the mean age among those reporting generalized body aches was 34.29 (± 10.99). There was a statistically significant difference in the age of the participants who suffered from fever compared to those who did not have fever (p= 0.014) as shown in Table 4.

Table 4. Age of the 79 studied subjects with post COVID- 19 vaccine complications.

Post vaccine complications	No.	(%)	Age			*p* value
			Min. – Max.	Mean ± SD.	Median	
Fever	37	46.8	21 - 50	30.86 (± 7.95)	29.00	0.014[1]*
Skin erythema	2	2.5	25 - 29	27.00 (± 2.82)	27.00	NS[1]
Headache	24	30.4	21 - 68	33.63 (± 12.52)	29.50	NS[1]
Generalized body ache	48	60.8	22 - 62	34.29 (± 10.99)	30.00	NS[1]
Cough	5	6.3	23 - 33	27.20 (± 4.02)	27.00	NS[1]
Dyspnea	2	2.5	24 - 51	37.50 (± 19.09)	37.50	NS[1]
Upper limb edema	1	1.2				
Vomiting	1	1.2	22 - 29	26.25 (±3.40)	27.00	NS[2]
Arm weakness	2	2.5				

[1] Independent T-test, [2] One Way ANOVA. *: *P* > 0.05 is not significant (NS).

The results of this study elaborated multiple factors related to serum IgG titers. There was a negative relationship between age and level of serum IgG with the highest titers of IgG in the youngest age group (20 – <35) years with a mean of 335.1±141.9 U/ ml as shown in Table 5.

Table 5. Relation between Serum IgG titer with age (years) in the 141 study subjects.

Age (years)	No.	Serum IgG titer (U/ml)		*p* value
		Mean ± SD.	Median (Min. – Max.)	
20 – <35	93	335.1 ± 141.9	366.0 (0.40 – 630.0)	
35 – 50	30	246.2 ± 151.2	288.0 (0.40 – 495.0)	0.013[H]
>50	18	332.9 ± 142.4	386.5 (25.80 – 508.0)	

Characteristic	Serum IgG (U/ml)	
	r	*p* value
Age	- 0.175	0.038[1]

SD: Standard deviation; H: H for Kruskal Wallis test; Statistically significant at $p \leq 0.05$; [1]Spearmen's correlation coefficient

Other factors as prior history of COVID-19 infection and type of received vaccine had also statistically significant effect on serum IgG antibodies titers as shown on Table 6.

Table 6. Univariate and multivariate linear regression analysis for the parameters affecting Serum IgG titer in the 141 studied subjects.

Parameters	Univariate analysis		#Multivariate analysis	
	p value	B (LL – UL 95%)	*p* value	B (LL – UL 95%)
Sex				
Female	0.407	20.815 (-28.645 – 70.275)		
Age (/years)				
20 – <35	0.031	56.386 (5.230 – 107.541)	NS	-18.677 (-91.530 – 54.177)
35 – 50	0.003	-88.545 (-146.918 – -30.172)	NS	-73.199 (-156.435 – 10.037)
>50	0.602	19.490 (-54.306 – 93.286)		
Residence				
Rural	0.280	30.130 (-24.747 – 85.006)		
Presence of Comorbidities	0.480	27.084 (-48.483 – 102.65)		
Presence of Hypertension	0.598	30.315 (-83.059 – 143.688)		
Presence of Diabetes Mellitus	0.772	15.636 (-90.888 – 122.16)		
Presence of Bronchial asthma	0.700	40.701 (-167.649 – 249.052)		
Presence of other Comorbidities	0.580	58.453 (-149.778 – 266.685)		
Vaccine type				
AstraZeneca	0.001	-83.495 (-131.464 – -35.526)	NS	-65.766 (-129.646 – -1.885)
Pfizer/the Moderna	0.943	-4.396 (-126.520 – 117.727)		
Sinopharm	0.198	43.357 (-22.963 – 109.678)		
Sinovac	0.015	62.143 (12.327 – 111.959)	NS	4.860 (-59.703 – 69.423)
COVID19 infection	0.031	54.276 (5.141 – 103.411)	NS	38.131 (-10.365 – 86.628)

B: Unstandardized Coefficients LL: Lower limit UL: Upper Limit

#: All variables with p<0.05 was included in the multivariate; *P* > 0.05 is not significant (NS).

Discussion

This study aimed to assess human IgG levels post-COVID-19 vaccination, among HCWs in Suez Canal University Hospital, and to detect short-term side effects post-vaccination. The study included 141 HCWs. The age of the studied subjects ranged from 21–68 years old with a mean of 55 ± 13.53 years. There was a negative relationship between age and level of serum IgG with the highest titers of IgG in the youngest age group (20 – <35) years with a mean of 335.1 ± 141.9 U/ ml.

These were similar to data reported in the study of Bayram et al., 2021 who found that men and women between the ages of 18 and 34 had the greatest seropositivity rates (88.9% and 79.5%, respectively).[11] However, Uysal et al., 2022 found that despite that there was no statistically significant correlation between age

and antibodies, people aged 30-39 (38.5%) had greater antibody titers than other age groups.[5]

The current study revealed that comorbid conditions were present in small percentages of HCWs (Table 6), as 5.7% were diabetics, 5% suffer from hypertension, and 2.8% had other chronic conditions (bronchial asthma, skin allergy, systemic lupus erythematous and thyrotoxicosis). None of these circumstances were remarkably correlated with serum IgG titer anti-spike seropositivity. This result agreed with that observed by El-Ghitany et al., 2022 study which reported similar results.[12]

This study observed that 96.5% of the studied samples had seropositive results post vaccination while only 3.5% were negative. In people who had previously been infected with COVID-19, some reports found a greater post-vaccination antibody response. Additionally, they suggested that in confirmed COVID-19 patients, one dosage of various vaccines might be sufficient. [13,14] The results of the current investigation were consistent with this concept since HCWs who had a clear history of prior COVID-19 infection had median and mean antibody titers of 347.44 and 370.00 U/ml and mean antibody positivity titers that were significantly higher. This was compatible with El-Ghitany et al., 2022 study which found that there was anti-spike titer variation between samples from people who had been infected previously (111.8) and those from the uninfected participants (39.8) ($p < 0.001$).[12]

In the current work, it was found that Oxford/AstraZeneca vaccine was the most frequent type received by HCWs (41.8%) followed by Sinovac (37.6%), Sinopharm (16.3%), Pfizer and Moderna (4.2%) including one nurse only of the participants who received Moderna vaccine.

In this study, it was found that the mean titer of anti-receptor binding domain IgG levels varied significantly amongst the various vaccine types, with the Sinovac vaccination group having the highest levels (354.66±115.98) post immunization. The second effective vaccine was Sinopharm vaccine with mean±SD (352.15±173.34) U/ml) and the highest titer 630.0 U/ml. In the current study, Pfizer and Moderna vaccines (m-RNA vaccines) were ranked third in efficacy (according to their titer, 311.7± 163.1 U/ml).

This study revealed that 62 of the participants (44%) reported no complications for post COVID-19 vaccines, while generalized body ache was the most common side effect post all vaccines (34%) irrespective of prior history of COVID-19 infection, followed by fever (26.2%) then headache (17%), respectively. Other non-significant side effects reported in this study included: cough, dyspnea, arm weakness, upper limb edema, and vomiting respectively. Similarly, a study from Wuhan by Zhu et al., 2020 showed muscle pain, headache, fatigue, and fever in vaccinated individuals by 17%, 39%, 44%, and 46%, respectively.[15]

With all vaccines, people who had historical signs of SARS-CoV-2 infection were more likely to experience side effects than those who did not. As example, generalized body ache occurred in Group A represented 47.5 % but in Group B it was only 24.4%. Also, other adverse effects like fever and headache represented higher rates in Group A than in Group B (30.5 % versus 23.2 % and 18.6% versus 15.9% respectively). These were compatible with findings of another study by Wise, 2021, who reported that both patient groups experienced identical localized injection side effects, such as edema or pain. However, systemic adverse effects such as fatigue headaches, chills, fever, and aches and pains in the muscles or joints were much more frequent in those with pre-existing immunity.[16]

This study demonstrated that there was a relationship between age and possible short side effects post vaccines especially fever as the most of participants who reported complications were in the age group below 50 years old. As the mean age of participants reporting fever was 30.86 (± 7.95), while the mean age among those reporting generalized body ache was 34.29 (± 10.99). This observation was also reported by another study done in Czech by Riad et al., 2021, revealed that the occurrence of adverse effects was marginally greater in the group ≤43 years old (94.8%) than in the group > 43 years old (91.5%).[16] Also, the type of vaccine was another factor in the current work determining the burden of short-

term side effects post-vaccination, as most of the participants who received Sinopharm vaccines had no complications representing 52.2%, followed by those who received Sinovac vaccine 50.9% followed by AstraZeneca then Pfizer and Moderna, respectively.

In this study, generalized body ache or fatigue was the most common short side effect between all vaccines, most common by Pfizer and Moderna vaccines representing 66.67% of those received these types. This was followed by headache, also reported by the group received Pfizer and Moderna vaccines representing 50%, then fever and cough represented 33.3% 16.6%, respectively. This was similar to another study by Kadali et al., 2021 who found that the main general symptoms were generalized fatigue, headache, chills, fever, sweating, dizziness and flushing, accounted for 58.9%, 44.8%, 35.9%, 22.04%, 9.22%, 8.34%, and 7.1%, respectively.[18]

In this study, the least vaccines causing short term side effects were the Sinovac and Sinopharm vaccines. These short-term side effects included: generalized body ache which was the most common (30.2% and 21.7%, respectively) among the vaccinated groups. This was followed by fever (24.5% and 30.4%, respectively), headache (15% and 13%, respectively), while 5.7% of those received the Sinovac vaccine complained of cough, 1.9% complained of dyspnea and two of them complained of gastrointestinal symptoms as vomiting and neurological symptoms as arm weakness. These were similar to findings of another study in Bangladesh by Mohsin et al., 2022, who found that the less side effects were detected in cases received Sinopharm (28%) and Sinovac (21.05%).[19]

In conclusion, there was a significant rising of serum IgG titer post vaccination. The current study reported higher post-vaccination antibody response in those previously infected with COVID-19. There were many factors determining the post COVID-19 vaccine serum IgG titers included: age, prior history of COVID-19 infection and type of vaccine. Also, age and type of vaccine determined the possible short side effects post vaccination.

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Author Contributions

SSS, NAN, FMA; Conception and design of the study. SSS, FMA, AEE; Acquisition of data. SSS, FMA, NAN; Laboratory or clinical/literature search. FMA, SSS; Analysis and interpretation of data collected. SSS, WHO, FMA, NAN; Drafting of the article and/or critical revision. All authors read and approved the final manuscript.

Declaration of Conflicting Interests

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Ethical approval

The study protocol was reviewed and approved by the Research Ethics Committee of the Faculty of Medicine, Suez Canal University (reference no. 4692, dated October 2021).

Informed consent

A written informed consent was obtained from each participant before being included in the study.

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