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Original Article

Microbiology Section

Immunity against COVID-19 in Vaccinated and Unvaccinated Individuals: A Prospective Cohort Study

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ABSTRACT

Introduction: Three years into the Coronavirus Disease-2019 (COVID-19) pandemic, questions linger regarding long-term vaccine efficacy, potential side effects, and the risk of future viral waves. Despite vaccinations, no existing vaccine offers complete protection, contributing to ongoing fears and vaccine hesitancy. Asymptomatic carriers and unattained herd immunity add layers of complexity. This study seeks to examine the status of immunity in vaccinated and unvaccinated individuals amidst the shifting landscape of different Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2) variants.

Aim: To determine the percentage of unvaccinated individuals who have developed COVID-19 specific antibodies and to compare the factors influencing immunity in both unvaccinated and vaccinated individuals.

Materials and Methods: This prospective cohort study was conducted at Sree Balaji Medical College and Hospital, Chennai, Tamil Nadu, India, from March 2021 to May 2023. Participants, aged 18-82 of both sexes, were divided into two groups. Group-1 comprised our college and hospital staff who were vaccinated, and Group-2 consisted of members from the local community in the Chromepet, Chennai area who remained unvaccinated. Blood samples were collected from both groups to assess immunity status. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS, version 22.0). The tests used included the Chi-square test, p-value, mean, and standard deviation.

Results: Blood group "B" was more commonly observed in Group-2. The prevalence of co-morbidities was higher in Group-2. Immunological markers CD4 and CD8 were below normal in some individuals in Group-2. By April 2022, 53 (95%) out of 56 persons in Group-1 and by December 2022, 24 (96%) out of 25 persons in Group-2 tested positive for COVID-specific IgG antibodies. By May 2023, 100% of the volunteers in both groups were found to be positive.

Conclusion: This study suggests that natural immunity may be effective in protecting against COVID-19. Whether vaccinated or not, by the end of the two-year study, all individuals in the study group had developed COVID antibodies.

Keywords: Co-morbidities, Immunoglobulin G, Pandemic

INTRODUCTION

The Coronavirus Disease 2019 (COVID-19) pandemic has swept across the globe, leaving behind a death toll in the millions and causing widespread panic since its initial report in December 2019. In an article published in The Lancet in 2022, it was stated that 18.2 million people died globally because of the COVID-19 pandemic between the beginning of the pandemic (1st January 2020) and the end of 31st December 2021[1].

Amid the growing sense of dread, the global scientific community, caught off guard by the onslaught of the virus, was left with no immediate remedies for treatment or prevention. In this situation, two primary groups of researchers emerged: one focusing on the development of a curative drug, and the other on developing a vaccine. Although several vaccines have been developed, questions about their long-term efficacy and potential side-effects remain. While the people in the world are indeed fortunate that the number of new COVID-19 cases appears to be declining, there is a lingering fear among us that the world could be struck by another wave of the virus at any time. The uncertainty remains. Are the health care providers better prepared for a potential resurgence? How many of us remain vulnerable to this threat?

When the vaccines became available for human use, there were many people opposing their use, citing side-effects and the lack of full protection because even vaccinated persons got infected. Some members of the press and media have exaggerated the side-effects, creating panic in the minds of many people about the side-effects. Many persons remained unaffected by the COVID-19 disease, whereas many people, after vaccination, got an infection. Hence, many people in society questioned the rationale for vaccination with the assumption of protecting human beings from COVID-19. This has prompted us to conduct a study to understand the difference between vaccinated persons and non-vaccinated persons.

The degree of protection conferred is a topic of ongoing research. Moreover, several cases of breakthrough infections have been reported, and fears about possible side-effects, exaggerated by sensational media news, have fueled vaccine hesitancy among certain segments of the population. This uncertainty has raised pertinent questions about the potential consequences of another virus wave on un-vaccinated individuals, as well as those who have not yet been exposed to the virus. During the period of this study, three waves of COVID-19 have passed through India, each with different variants.

Some results suggest that vaccine-induced immunity is more effective. Other results suggest that natural immunity is more effective, and some have shown equal effectiveness of both. Yu Y et al., have stated that there was no trend of decreasing Receptor-Binding Domain (RBD) antibodies in those with natural immunity for upto nine months [2]. Townsend JP et al., have stated that their findings provide quantitative evidence supporting booster vaccination as a crucial approach toward the curtailment of breakthrough infections and reinfections [3]. Pilz S and Loanidis JPA, have stated that frequent boosters may no longer be necessary for the majority of the population but only for certain risk groups, for example, the elderly, and in particular long-term care residents [4]. Sciscent BY et al., state that immunity to SARS-CoV-2 involves antibody responses, but the variable length of protection permits the possibility of reinfection. In the current scenario,

vaccinations will play a major role as we are exploring more about the reinfection mutations of the SARS-CoV-2 virus [5]. Milne G et al., have stated that the coordination between the two types of adaptive immune response is likely to be important to mitigate the most severe consequences of infection. Populations of specific memory B cells and T cells remain stable or even increase in size many months after SARS-CoV-2 exposure; compared with the immune response to natural infection, vaccination elicits a response of greater magnitude and higher specificity, largely focused on the RBD. They have also stated that upon natural infection, the T cell-mediated response appears to be targeted across a larger variety of epitopes than the humoural response [6]. In the document from GOV.Wales, it is stated that a previous COVID-19 infection typically results in a stronger immune response than vaccination [7]. Thus, there are reports supporting both immunity following infection as well as immunisation. Such reports have inspired us to conduct a study in this area.

The aim of the study was to determine the percentage of unvaccinated individuals who have developed COVID-specific antibodies and to compare the factors influencing immunity in both unvaccinated and vaccinated individuals.

MATERIALS AND METHODS

This is a prospective cohort study conducted at Sree Balaji Medical College and Hospital, Chennai, Tamil Nadu, India. The study period was from March 2021 to May 2023.

This study is part of a detailed and extensive analysis as the authors have undertaken to examine various aspects of immunity in both vaccinated and unvaccinated individuals. The study was conducted on volunteers after obtaining Institutional Human Ethical Committee clearance from Sree Balaji Medical College (No. 002/SBMC/IHEC/2021/1528 dated 12.03.2021) and written informed consent from the volunteers. All the participants were thoroughly examined before being accepted for the study. A detailed proforma was also used to record comprehensive history and all the findings.

Inclusion criteria: All volunteers above 18 years of age, of both sexes were included in the study.

Exclusion criteria: The RT-PCR-positive individuals for COVID-19 or those clinically diagnosed with the disease, those on immunosuppressive therapy and the ones known cases of immunodeficiency were excluded from the study.

Sample size calculation: The sample size was calculated based on the previous Coronavirus infection survey (antibodies data) from March 14 to 20, 2022, in Wales [7]. The percentage of people testing positive for antibodies at the standard threshold ranged from 97.5% to 99.7% among subjects, with a 95% confidence limit and 7% relative precision of estimate using the following formula:

$$\text{Formula for sample size calculation}=\frac{(Z)^2\times(1-p)}{(p)\times(e)^2}$$

Where: Z=1.96, prevalence of positive=97.5, Precision (e)=7%

$$\text{Sample size (N)}=\frac{(1.96)^2\times(1-0.975)}{0.975\times(0.07)^2}$$

$$=\frac{3.84\times0.025}{0.01868}=21$$

Procedure

For this study, 25 unvaccinated volunteers were accepted.

For this specific study, blood samples were taken from two groups of people.

Group-1: These volunteers were our college and hospital staff, who were prepared to get vaccinated. They came for vaccination from March 2021 onwards. Covishield vaccine was given at 0, 3, and 12 months after registration. Blood samples were taken before giving the vaccine and at 26 months after the registration. The number of dropouts increased after each blood sampling, and only 56 remained committed to this research until the end and gave the 4th sample of blood in May 2023.

Group-2: These volunteers were from the local community in Chromepet, Chennai, who were not willing to take the vaccine and remained unvaccinated until December 2022.

In the first group, 154 individuals were initially accepted/registered for vaccination. Blood samples were taken for various tests, including Complete Blood Count (CBC), C-Reactive Protein (CRP), COVID-specific IgG, IgM, and CD3, CD4, CD8 and CD45. They were then given the Covishield vaccine and observed, with further vaccinations at three months and 12 months after registration. Blood tests were conducted as described above, and at 26 months as well.

The normal levels of Clusters of Differentiation (CD) markers were provided by HCG Anderson Laboratory, Chennai, which conducted the tests based on the MOU signed by our institution and the laboratory:

- Normal levels of CD3+ Absolute count (T lymphocytes)=600-2500
- Normal levels of CD4+ Absolute count (T helper cells)=400-1500
- Normal levels of CD8+ Absolute count (T suppressor cells)=200-1100
- Normal levels of CD45+ Absolute lymphocyte count=1000-3000

The second group consisted of 25 volunteers from various areas in the local community in and around Chromepet, Chennai, and they were not hospital staff. None of them had any definite and specific complaints suggestive of COVID-19 before or after registration. These volunteers were also subjected to all the tests performed on the first group. They were tested first in December 2022.

A Complete Blood Count (CBC) was performed using a 5-part Haematology Analyser (BC 6000 Mindray) based on the electrical impedance principle. Erythrocyte Sedimentation Rate (ESR) was measured using the Vescube 30 Touch employing the modified Westergren method. C-reactive protein was determined by the Nephelometric Technique. Immunoglobulins IgG and IgM specific for SARS-CoV-2 assay (BIOMERIEUX) were examined using the Enzyme-Linked Fluorescent Assay (ELFA) technique. This assay helps determine if the individuals may have been exposed and infected by the virus and if they have mounted a specific anti-SARS-CoV-2 IgG immune response. The assay principle combines a two-step sandwich enzyme immune assay method with final fluorescent detection. All the assay steps are automatically performed by the instrument (VIDAS). The SARS-CoV-2 IgG test targets RBD/S protein, with excellent correlation to the WHO International standard in BAU/mL (Binding Antibody Units/mL). The report of anti-SARS-CoV-2 IgG (SPIKE-S1-RBD) was generated by ELFA technology (mini VIDAS/VIDAS). The CD counts were determined by Flow Cytometry at the HCG Anderson Laboratory, Chennai, with which the authors have an MOU. The results were expressed in 10^6/L units.

STATISTICAL ANALYSIS

Demographic variables in categorical/dichotomous form were provided with their frequencies and percentages. Mean and standard deviation were used to present CD3, CD4, CD8, CD45 counts, and IgG levels. Group-specific comparisons for age, sex, CD counts, co-morbidity, and blood group distribution were performed using the chi-square test. A p-value of ≤0.05 was considered statistically significant, and two-tailed tests were employed to assess significance. Statistical analysis was conducted using SPSS, version 22.

RESULTS

The age of the participants in this study ranged from 18 years to 74 years in Group-1 and from 19 years to 82 years in Group-2. The majority of participants in both groups were below 40 years of age, as shown in [Table/Fig-1].

Age group (Years)	Groups				Chi-square test
	Group-1 (N=56)		Group-2 (N=25)		
	N	%	N	%	
18-40	30	53.57%	11	44.00%	χ^2=13.49 **p=0.001*****
41-60	23	41.07%	5	20.00%	
>60	3	5.36%	9	36.00%	
Total	56	100.00%	25	100.00%	

[Table/Fig-1]: Age distribution in study population.
Chi-square test p <0.001 Significant; S=significant

In Group-1, a greater number of females participated in the study than males, but in Group-2, the distribution of males and females was equal [Table/Fig-2].

Sex	Groups				Chi-square test
	Group-1 (N=56)		Group-2 (N=25)		
	N	%	n	%	
Male	7	12.50%	13	52.00%	χ^2=14.50 **p=0.001*****
Female	49	87.50%	12	48.00%	
Total	56	100.00%	25	100.00%	

[Table/Fig-2]: Sex distribution in study population.
Chi-square test, p≤0.001 significant

Among the cases studied, although the percentage of Christians and Muslims appears to be lower in both groups compared to the percentage of Hindus in the general population of Tamil Nadu State, it was not statistically significant [Table/Fig-3]. Normal values for the general population are given in reference [8].

Religion	General population in Tamil Nadu [8]	Group-1 (n=56)	Group-2 (n=25)
Hindu	88%	43 (76.79%)	18 (72.00%)
Muslim	6%	6 (10.71%)	4 (16.00%)
Christian	6%	7 (12.50%)	3 (12.00%)

[Table/Fig-3]: Comparison of Religion distribution in study population with general population in Tamil Nadu.
Chi-square test p>0.05 not significant
χ^2=0.45 p=0.80

Among the volunteers in Group-1 and Group-2, the majority of individuals in Group-2 had B group blood [Table/Fig-4]. Normal values for the general population are given in reference [9].

Blood group	In General population in Tamil Nadu [9]	Group-1 (n=56)	Group-2 (n=25)
O	40.09%	22 (39.29%)	10 (40.00%)
A	25.57%	13 (23.21%)	2 (8.00%)
B	29.79%	17 (30.36%)	13 (52.00%)
AB	4.55%	4 (7.14%)	0.00%

[Table/Fig-4]: Comparison of blood group distribution in study population with general population in Tamil Nadu.
Chi-square test p>0.05 not significant
χ^2=6.13 p=0.10

The individuals in Group-2 had more co-morbidities [Table/Fig-5]. The reason why individuals in Group-2 have not taken vaccines may be due to the illnesses they were suffering from and the fear of death due to the deterioration of their conditions following vaccination, as per their assumption.

The CD test in both groups revealed that in Group-2, many participants had lower CD4 and CD8 counts [Table/Fig-6]. The comparison of IgG levels in both groups is shown in [Table/Fig-7]. In fact, by May 2023, all vaccinated and unvaccinated members in this study group had tested positive (100% positive in both groups).

In Group-1, the lowest IgG level was 215 BAU/mL, the highest IgG level was 927 BAU/mL, and the mean IgG level was 617.12 BAU/mL in May 2023.

Co-morbidity	Group-1 (n=56)	Group-2 (n=25)
Diabetes	6 (10.71%)	2 (8.00%)
Asthma	2 (3.57%)	2 (8.00%)
Heart disease	0 (0.00%)	2 (8.00%)
Diabetes+Hypertension	0 (0.00%)	2 (8.00%)
Others	5 (8.92%)	3 (12.00%)
No co-morbidities	43 (76.78%)	14 (56.00%)

[Table/Fig-5]: Comparison of presence of Co-morbidities in both the groups.
Chi-square test, p≤0.05 significant
χ^2=11.00 Co-morbidity is less in Group-1

Blood tests	Group-1 (n=56)			Group-2 (n=25)			Chi-square test
	Normal (%)	Above normal (%)	Below normal (%)	Normal (%)	Above normal (%)	Below normal (%)	
CD3+	42 (75.00%)	10 (17.86%)	4 (7.14%)	21 (84.00%)	3 (12.00%)	1 (4.00%)	χ^2=0.82 p=0.66
CD4+	43 (76.79%)	8 (14.29%)	5 (8.93%)	14 (56.00%)	3 (12.00%)	8 (32.00%)	χ^2=6.86 **p=0.03***
CD8+	51 (91.07%)	2 (3.57%)	3 (5.36%)	19 (76.00%)	0 (0.00%)	6 (24.00%)	χ^2=6.75 **p=0.03***
CD45+	40 (71.43%)	16 (28.57%)	0 (0.00%)	21 (84.00%)	4 (16.00%)	0 (0.00%)	χ^2=1.46 p=0.22

[Table/Fig-6]: Comparison of presence of CD counts in both the groups.
Chi-square test
CD3=χ^2=0.82 p=0.66(NS). CD4=χ^2=6.86 p=0.03*(S) "below normal" high in Group-2
CD8=χ^2=6.75 p=0.03*(S) "below normal" high in Group-2. CD45=χ^2=1.46 p=0.22(NS)

Group	Period	% Positive for COVID specific IgG	Lowest IgG (BAU/mL) level	Highest IgG (BAU/mL) level	Mean IgG (BAU/mL) level
Group-1	April 2022	95%	0	721	149.85
	May 2023	100%	215	927	617.12
Group-2	December 2022	96%	45.70	777.20	347.44
	May 2023	100%			

[Table/Fig-7]: IgG levels in Group-1 and Group-2.

In Group-2, the lowest level was 45.70, the highest level was 777.20, and the mean IgG level was 347.44 in December 2022.

In the 1st group, by April 2022, 53 (95%) of the volunteers had become positive for COVID-specific IgG antibodies, and by May 2023, all 100% had become positive. In the 2nd group, during their first test in December 2022, 24 (96%) were found to be positive for COVID-specific IgG antibodies, and by May 2023, all 100% had become positive for COVID-specific IgG.

The main reason for vaccine hesitancy in Group-2 seems to be the fear of death due to vaccination [Table/Fig-8]. Moreover, this observation indicates that there is a higher prevalence of co-morbidities among Group-2 participants. Hence, they will be all the more scared to take the vaccine, fearing an exacerbation of their disease and subsequent death.

Reasons for hesitancy	Numberof participants	Percentage of participants
Fear of death	10	40.00%
Fear of side-effects	7	28.00%
Indifference/Not bothered	3	12.00%
Fear of pain	2	8.00%
Religious belief	1	4.00%
Others	2	8.00%
Total	25	100.00%

[Table/Fig-8]: Reasons for vaccine hesitancy in Group-2.

In Group-2 participants, the eosinophil count and platelet count are high in a few of them. The basophil count is low in many participants [Table/Fig-9]. The influence of coronavirus infection/COVID vaccines

on the blood cells in asymptomatic persons has not been fully understood.

	Normal		Above normal		Below normal	
Blood cells	**n**	**%**	**n**	**%**	**n**	**%**
TWBC	20	80.00%	5	20.00%	0	0.00%
Polymorph	20	80.00%	5	20.00%	0	0.00%
Lymphocyte	22	88.00%	0	0.00%	3	12.00%
Eosinophil	21	84.00%	4	16.00%	0	0.00%
Basophil	1	4.00%	0	0.00%	24	96.00%
Monocyte	18	72.00%	0	0.00%	7	28.00%
Platelets	22	88.00%	3	12.00%	0	0.00%

[Table/Fig-9]: Complete Blood Count (CBC) among Group-2 participants.

DISCUSSION

This study started in March 2021 and ended in May 2023. The authors registered two groups of volunteers. One group consisted of 154 volunteers from our college and hospital who wanted vaccination, but only 56 volunteers could complete the study. The other group consisted of 25 volunteers from the local community in Chrompet, Chennai, who did not want to get vaccinated.

In this study, the percentage of volunteers in Group-2 with blood group 'B' was higher compared to the distribution of blood groups in the general population. CD4 counts and CD8 counts were low in a significant number of volunteers in the 2nd group, and the reasons are not clear. The number of persons with co-morbidities was also higher in the Group-2 volunteers. So far, a consensus has not been reached among scientists regarding the level and duration of protection offered by infection, the vaccine, or both (hybrid).

Altarawneh HN et al., stated in NEJM that no notable differences have been observed in the effectiveness against BA.1 and BA.2 of previous infection, vaccination, and hybrid immunity [10]. Shenai MB et al., reported that there is currently no statistical advantage to vaccination in the COVID-naive compared to natural immunity in the COVID-recovered; unvaccinated COVID-recovered individuals should be considered to have atleast equal protection to their vaccinated COVID-naive counterparts [11]. Vespa S et al., reported that vaccination and natural infection are both successful in inducing the clearance of the virus, also guaranteeing better COVID-19 outcomes [12]. Franchi M et al., reported in the Journal of Infection and Public Health that there is equivalence of protection from natural immunity in COVID-19 recovered versus fully vaccinated individuals; this was observed during both periods in which delta or omicron were the dominant variants [13].

Diani S et al., have stated that previous SARS-CoV-2 infection provides greater protection than that offered by the single or double/triple-dose vaccine. They also state that the protection from infection conferred by the vaccination cycle is very good after 14 days; however, it tends to decline rapidly over the following months, nearly disappearing about five months after the 2nd dose. They state that due to the documented prolonged immune response after COVID-19, further administration of vaccine doses, especially from the second onwards, does not lead to a significant improvement in immunity. They reiterate that there is no need for vaccine administration in those who have recovered from COVID-19 [14].

Piler P et al., in their study between October 2020 and March 2021 in the Czech population, state that by the end of March 2021, the seropositivity rate reached 50% in their study subjects, which corresponded with their government data [15]. Alejo JL et al., have stated that in their cross-sectional study of unvaccinated US adults, antibodies were detected in 99% of individuals who reported a positive COVID-19 test result, in 55% of those who believed that they had COVID-19 but never tested, and in 11% who believed they had never had a COVID-19 infection [16]. Jones JM et al., have stated that the incidence of first-time SARS-CoV-2 infection was lower among vaccinated persons [17]. According to the document downloaded from GOV.WALES, a previous COVID-19 infection typically results in a stronger immune response than vaccination. To achieve a similar level of protection from vaccination alone, a higher concentration of antibodies is needed. It is also stated that between 14 and 20 March 2022, over 9 in 10 persons aged 16 and over tested positive for antibodies to the coronavirus (COVID-19) from a blood sample (95% credible interval: 99.1% to 99.6%) [7]. Mishra BK et al., state that the development of antibodies following natural infection not only protects against reinfection by the virus to a great extent but also safeguards against progression to severe COVID-19 disease [18]. Biggs AT and Littlejohn LF, state that risk exposure, reliability, and sustainment support building public health policy around vaccines as the safest option [19]. In this study, the authors found that after two doses of the vaccine, the antibodies remained high for about two years after the 2nd dose.

Zhang S et al., from China, have reported that they have not observed a significant difference in antibody levels between the age groups of 20-60 years and 60 years and above. They have also stated that people vaccinated with one dose of an inactivated vaccine produced higher levels of antibodies than unvaccinated individuals, which was similar to those who received two doses [20].

Meyers J et al., state that individuals fully vaccinated with mRNA vaccine mounted strong humoural immunity with much higher anti-RBD1, anti-S1, and anti-S2 antibody levels compared to the naturally infected individuals [21]. Wong RSY et al., concluded in her article that achieving herd immunity through natural infection is ludicrous, and vaccination is a practical way forward [22]. Khalife J and VanGennep D, state that pursuing herd immunity without a vaccine involves numerous uncertainties, is costly in terms of lives and disease, is ineffective, and unethical and uncompassionate [23]. The present study shows that whether vaccinated or not vaccinated, all the people now have COVID-19 antibodies. Another study of the authors has shown that T cell responses are also good in vaccinated persons [24]. Nordstrom P et al., state that vaccines are associated with a reduction in the transmission of the SARS-CoV-2 virus within families, which likely has implications for herd immunity and pandemic control [25]. Addo IY et al., in their article have said that vaccine-induced protection wanes over time, thereby necessitating booster doses. The waning of vaccine-induced protection against SARS-CoV-2 usually begins from 3 to 24 weeks after receiving a full dose [26]. This is contrary to the present study in which it is observed that the antibody levels have not come down even two years after the 2nd dose of the vaccine (26 months after the 1st dose). Karachaliou M et al., state that previously infected people mounted higher antibody levels after the 1st and 2nd doses than naive individuals [27]. Goldberg Y et al., report that waning immunity was evident in all age groups, and that persons with hybrid immunity were better protected against re-infection than uninfected persons who had previously received 2 doses of the vaccine [28].

Pooley N et al., in their article, have stated that post-infection antibody dynamics show a slower decline than post-vaccination titers; asymptomatic or mild infections may not provide robust protection; antibodies elicited by currently available vaccines and prior infections with older variants are not as effective at neutralising new VOC, especially Omicron. The T cell response to both vaccination and prior infection is more long-lasting than the antibody response [29]. Sekine T et al., have stated that SARS-CoV-2-specific memory T cells will likely prove critical for long-term immune protection against COVID-19 [30]. Another study of the authors has shown that the T cell responses were also good in the vaccinated [24]. In all of the studies, the IgG levels were also high, proving that humoural immunity and cellular immunity were good following vaccination and worked hand in hand in the vaccinated individuals. At the same time, in the unvaccinated individuals, the IgG levels were also very good (high). Probably, the T cell response

may also be good in them. Grant A and Hunter PR, in their article have stated that if herd immunity is not achieved, then those people who have not taken the vaccine will remain at risk of severe illness and death [31]. AbdAllah M and Cordie A, defined herd immunity as the indirect protection from infection conferred to susceptible individuals when a sufficiently large proportion of immune individuals exist in a population [32]. Fajar JK et al., in their study, have estimated the global prevalence of COVID-19 vaccination hesitancy at 25%. They say that older people who are more than 50 years, those living with children at home, individuals who have ever tested for COVID-19, and those with a history of influenza vaccination had a lower incidence of vaccination hesitancy, and in contrast, single marital status and unemployment are associated with an increased incidence of vaccination hesitancy [33].

Buss LF et al., state that seroepidemiological, molecular, and genomic surveillance studies in the region are required to determine the longevity of population immunity, the correlation with the observed antibody waning, and the diversity of circulatory lineages. Monitoring of new cases and the ratio of local versus imported cases will also be vital to understand the extent to which population immunity might prevent future transmission, and the potential need for booster vaccinations to bolster protective immunity [34]. Fontanet A and Cauchemez S, opined that herd immunity could be achieved with only 50% population immunity [35].

Ninety-five percent of the volunteers tested positive nine months after the 2nd dose of the Covishield vaccine (i.e., 12 months after the 1st dose). One hundred percent of the volunteers tested positive 14 months after the 3rd dose of the vaccine, approximately 2 years after the 2nd dose, and 26 months after the 1st dose. In the 2nd group of volunteers from the local community who had not taken any vaccine and remained asymptomatic until December 2022, the positivity rate was 96%. When we tested again in May 2023, all 100% of them had tested positive. So, by May 2023, both vaccinated (Group-1) and unvaccinated (Group-2) groups had tested positive for antibodies. The present study shows that now all the vaccinated individuals as well as the unvaccinated ones show antibodies.

Regarding certain factors influencing immunity against COVID-19, such as age, sex, co-morbidity, vaccination status, etc., various views have been discussed, and these factors in the present study groups have also been tested and compared.

Limitation(s)

This study was conducted among persons living in and around Chennai. This may not fully reflect the status of people in other areas. Multicenter studies will provide us with more information.

CONCLUSION(S)

The present study on immunity in vaccinated and unvaccinated individuals suggests that by May 2023, both vaccinated and unvaccinated persons have tested positive for COVID-specific IgG antibodies. Natural immunity may be effective in protecting against COVID-19. It is observed that all unvaccinated individuals in the study had developed COVID-specific antibodies before May 2023, but none of them had any symptoms of the disease. Age, sex, and co-morbidities exert some influence on the development of COVID-specific antibodies. Natural immunity may be able to protect us from COVID-19, even in the absence of any further vaccination.

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