ISSN 2475-5451

Research Article

International Journal of Diabetes & Metabolic Disorders

Anti-Spike Antibody Responses to Covid-19 Vaccine 3 Doses in Health Care Workers Working in Acute Care Hospital in Myanmar

Khin Phyu Pyar[1]*, Zar Ni Htet Aung[2], Sai Aik Hla[2], Soe Win Hlaing[2], Soe Min Aung[2], Nyan Lin Maung[2], Thein Tun Myint[2], Kyaw Thet Maung[2], Aung Thu[2], Han Lin Aung[3], Thurein Wynn[3], Aung Phyo Kyaw[3], Saw Thar Wah[2], Myo Thant Kyaw[3], Zay Phyo Aung[3], Sit Min[3], Myat Ko Ko[4], Kaung Myat Oo[4], Htet Aung[4], Thi Han Tun[5]

[1]Professor and Head/ Senior Consultant Physician, Department of Medicine/ Department of Nephrology, Defence Srevices Medical Academy/ No. (1) Defence Services General Hospital (1000 Bedded)

[2]Consultant Physician, No. (1) Defence Services General Hospital, (1000 Bedded)

[3]Assistant Lecturer, Department of Medicine, Defence Srevices Medical Academy

[4]Consultant Pathologist, No. (1) Defence Services General Hospital, (1000 Bedded)

[5]Public Health Specialist, No. (1) Defence Services General Hospital, (1000 Bedded)

***Corresponding author:**
Khin Phyu Pyar, Professor and Head/ Senior Consultant Physician, Department of Medicine/ Department of Nephrology, Defence Services Medical Academy/ No. (1) Defence Services General Hospital (1000 Bedded), Myanmar.

Submitted: 22 Sep 2022; **Accepted**: 29 Sep 2022; **Published**: 07 oct 2022

Citation: *Khin Phyu Pyar, Zar Ni Htet Aung, Sai Aik Hla, Soe Win Hlaing, Soe Min Aung et al. (2022). Anti-Spike Antibody Responses to Covid-19 Vaccine 3 Doses in Health Care Workers Working in Acute Care Hospital in Myanmar. Int J Diabetes MetabDisord, 7(2), 201-209.*

Abstract

Background

The health care workers are prone to COVID-19 infection as they are working in front line; thus, they are in priority groups for vaccination. This study aimed to assess the level of anti-Spike antibody 2 weeks after 3 doses of COVID-19 vaccine among health care workers (HCW).

Methods

A cross-sectional descriptive study was conducted in July 2022 among health care workers (HCW) who received COVID-19 vaccine 3 doses. Data were collected by using standardized forms and analysis was done.

Results

A total of 42 HCW were included; the mean anti-Spike antibody level was 3734.19 U/mL. Female had higher anti-Spike antibody level than male, 4857.67 U/mL and 3427.78 U/mL respectively. HCW with diabetes mellitus had significantly higher anti-Spike antibody level 6740.00 U/mL than those without diabetes mellitus 2884.00 U/mL. Anti-Spike antibody level in smokers (3376.42 U/mL) was lower than that of non-smoker (3845.99 U/mL). HCW with history of COVID-19 infection had higher anti-Spike antibody level (4013.79 U/mL) than that of those without infection (3524.48 U/mL); those with history of COVID-19 infection in fourth wave (The Omicron outbreak; 6 months ago) had higher antibody level (4013.79 U/mL) than that of those with history of infection in third wave only (The Delta outbreak; one year ago) (3524.48 U/mL). HCW who got vaccinated in the afternoon had higher antibody level (4350.77 U/mL) than who got in the morning (2912.07 U/mL). Negative relation was detected between time from last vaccination to anti-Spike protein antibody level though it was not statistically significant. Significant predictors for anti-Spike antibody level on univariable analysis were BMI and presence of diabetes.

Conclusions

Anti-Spike antibody level was significantly related with BMI and diabetes mellitus; those with high BMI and diabetes mellitus had higher level of antibody. Anti-Spike antibody level was relatively higher in female; non-smokers; those with COVID-19 infection particularly in fourth wave (The Omicron infection); those with shorter duration from last vaccination; and those who got vaccination in the afternoon although it was not significant statistically.

Keywords: Anti-Spike protein antibody, COVID-19, vaccination, health care workers (HCW)

Background

Vaccine program has been launched in Myanmar since January 2021; Covaxin and Covishield were the two main vaccines available initially. Later, Sinopharm, Sinovax, Sputnik, Pfizer, Moderna, Johnson and Johnson has been accessible. First, two doses were given with the interval of 4-6 weeks. All the HCW were considered as at risks group and given vaccination in priority group; first dose of vaccine in January/February 2021 and second dose in March/April 2021. Third and fourth doses were given 5-6 months apart depending on availability of vaccine. As of early April 2021, 50% of total population of Myanmar got one dose; and, 40% of total population received 2 doses of vaccine. In August 2021, 50% of total population of Myanmar got two doses [1]. Booster vaccination was given to high-risk persons like HCW.

Vaccine stimulates the individual to produce protective antibody level. It begins few days after vaccination; then, the level continues to rise till 6 months. The protective antibody response, both quantity and quality, was found to be better in vaccinated individuals than that of natural infection; vaccination elicits robust SARS-CoV-2-specific immune memory regardless of prior infection. The antibody level was 17 times higher in mRNA vaccinated individuals; therefore, the neutralization activities was better than those from natural infections [2]. The neutralizing activity of vaccine-elicited antibodies was more targeted to the receptor-binding domain (RBD) of the SARS-CoV-2 spike protein compared to antibodies elicited by natural infection [3, 4]. The combination of a previous SARS-CoV-2 infection and vaccination, hybrid immunity, seemed to confer the greatest protection against SARS-CoV-2 infections [5, 6]. Regarding duration of protectivity, infection-acquired immunity boosted with vaccination lasted more than 1 year after infection [7, 8].

The efficacy varies with type of vaccine; 70% for Covaxin, 90% for Covishield, and 94% for Sputnik V and Sputnik Light. The immunity was said to be lasted for 6 months. Clinical efficacy had been mentioned in several studies. The clinical efficacy of Covaxin was 81% in Bharat Biotech report [9]. Sinopharm and Sinovax are similar to Covaxin. Covidshield is structurally similar to AstraZeneca. Efficacy at preventing disease by AstraZeneca was 85% [10]. A large-scale study in India armed forces following completed Covishield vaccine revealed nearly 93% reduction in prevalence of Covid infections; and, reduction in COVID-related deaths by 98 % [11]. The protective effect of Sputnik V was 94%; Johnson and Johnson were 98%.

SARSCoV2 virus has been mutating producing new strain, new variant and subtype; new strain alters the efficacy of vaccine. The effect of Covaxin on alpha & delta strain became low it was 68% to 78% in one study [10, 12]. Studies from different countries mentioned vaccine effectiveness against severe disease and mild disease [13]. The protective efficacy as well as the duration of protection was changing. Not only the findings from England but also from US confirmed that second booster (fourth dose) had high protection rate 80% in first 6 months; the duration of protection waned over time [15]. In recent CDC report, after the first booster shot, vaccine effectiveness against severe illness with Omicron variants was 68% in the first six months; then, it declined to 52% after 6 months [14].

The time of the day of vaccination determines antibody response because of circadian clocks in the adaptive immune response [16]. The magnitude of the anti-Spike antibody response was found to be associated with the time of day of vaccination, vaccine type, age, sex, and days post-vaccination [17]. They also pointed out the importance of timing; HCW who received the SARS-CoV-2 vaccine in the afternoon had higher antibody level than those who were vaccinated in the morning [17].

Breakthrough infection (BTI) among HCW was reported globally because they were the front-line workers in COVID-19 pandemic [18, 19, 20, 21]. The prevalence of breakthrough infection varied from one country to another; it differed even within same country with same vaccine with different study site [19, 22, 23]. Previous report from Myanmar revealed that one in four physicians who had two doses of vaccine had BTI [24]. Moreover, BTI due to the Omicron variant were found in early 2022 in Myanmar [25]. Therefore, the data on the anti-Spike antibody which directly reflected the protective efficacy of 3 doses of COVID-19 vaccine in health care workers working in acute care hospital was urgently required in Myanmar. Therefore, this study aimed to assess the level of the anti-Spike antibody to 3 doses of COVID-19 vaccine among health care workers (HCW) who were working in acute care hospital in Yangon, Myanmar.

Methods

Study design and population

A cross-sectional descriptive study was conducted in July 2022. HCW working in acute care hospital who had 3 doses of COVID-19 vaccine, the last dose at least 2 weeks ago was included after getting informed consent. This study was approved by the Hospital Research and Ethics Committee of No.(1) Defence Services General Hospital (1000-Bedded) Megalodon, Yangon.

Data collection and procedure

Demographic characteristics (sex, age, height, weight, smoking status) and comorbidity (hypertension, diabetes mellitus) were collected using a standardized case report form. The name of each COVID-19 vaccine, date of each vaccination, timing of the day of vaccination of the last dose, timing of SARS-CoV-2 infection, and, blood level of anti-Spike antibody was recorded. The data were checked by two medical officers and then, supervision, completeness, and consistency of collected data were performed by the principle investigator.

Anti-Spike antibody was measured according to 'Double-antigen sandwich principle'. Total duration of assay was 18 minutes. For first incubation, 20 µL of sample, biotinylated SARS CoV 2 S RBD specific recombinant antigen and SARS CoV 2 S RBD specific recombinant antigen labeled with a ruthenium complex) were done to form a sandwich complex. Then, second incubation was performed after addition of streptavidin-coated microparticles, the complex becomes bound to the solid phase via interaction of biotin and streptavidin. The reaction mixture was aspirated into the measuring cell where the microparticles were magnetically captured onto the surface of the electrode. Next, unbound substances were removed with ProCell/ProCell M. Later, application of a voltage to the electrode to induce chemiluminescent emission was done; it was measured by a photomultiplier. Finally, the results were determined via a calibration curve, instrument specifically generated by 2 point calibration; and, a master curve was provided via the reagent barcode or e barcode. These samples were measured by using Cobas E411 immunoassay analyzer.

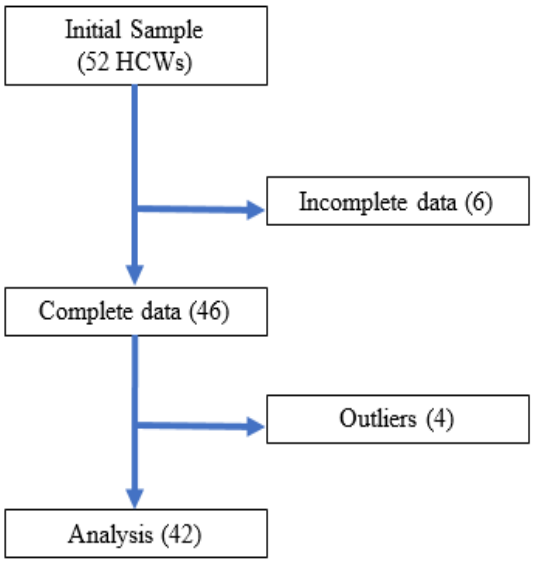
Working Definition

Body mass index (BMI) was a person's weight in kilograms divided by the square of height in meters, an indicator of body fatness. BMI was categorized as underweight (<18.5 kg/m^2), normal weight (18.5 to 24.9 kg/m2), overweight (25.0 to 29.9 kg/m^2) and (≥30.0 kg/m^2) obese. Comorbidity was a presence of more or additional medical conditions or diseases in COVID-19 patients.

Smoking status was classified into smoker and non-smoker. Smoker was defined if HCW was still smoking at the time of estimation of blood test irrespective of duration of smoking. Nonsmoker was defined if HCW stopped smoking at the time of estimation of blood test irrespective of duration of quitting.

History of COVID-19 infection was defined if HCW had signs and symptoms of COVID-19 infection with positive nasopharyngeal swab tests either with rapid test or PCR method.

Algorithm



Statistical Analysis

Total samples of 42 HCW were analyzed by SPSS version 26.0 for MacOS. Descriptive statistics was done, continuous variables were assessed normality by Shapiro-Wilk test. Normally distributed data were expressed in mean ± SD and non-normal data were expressed as Median (IQR). Categorical data were expressed in frequency and percentage. Antibody differences between sex, and history of covid infection, smoking and time of vaccination were compared by independent t test, BMI groups by one-way ANOVA test and expressed in mean ± SD, and differences between diabetes status were assessed by Mann-Whitney U test. Univariable and multivariable analysis was used by linear regression. P value < 0.05 was used as significant level.

Results

Final analysis was done in 42 HCW. The proportion of different types of vaccine received by HCW were Covaxin 88%, Sinopharm 70%, Covishield 84% and Sputnik V 30%. Table (1) demonstrates baseline characteristics. The mean age was 40.55 ± 8.93 years; the youngest was 21 years and the eldest was 63 years. Most of them were male; male 33 (78.6%) and female 9 (21.4 %). The median BMI and (IQR) were 24.30 (22.51 – 26.64) kg/m^2; the lowest BMI was 18.7 kg/m^2 and the highest was 40 kg/m^2. Nine HCW (21.4%) had comorbidity; seven HCW (16.7 %) had type 2 diabetes mellitus. Ten HCW (23.8 %) were smokers. Eighteen HCW (42.9 %) had history of covid 19 infection; and, the median duration from last known infection was 189.00 days (IQR; 177.00 – 397.25). Median duration from last vaccination was 86.00 (IQR, 29.25 – 141.00) days. Regarding time of the day of vaccination, 18 HCWs (42.9 %) were vaccinated in the morning and 24 (57.1 %) in the afternoon. The mean anti-Spike antibody level was 3734.19 ± 2470.43.

Table (1) Baseline characteristics of HCW (n=42)

Characteristics	Descriptive data
Age (yr) (Mean ± SD)	40.55 ± 8.93
Female, n (%)	9 (21.4)
BMI (kg/m2) (Median, IQR)	24.30 (22.51 – 26.64)
Comorbidity, n (%)	9 (21.4)
Diabetes mellitus, n (%)	7 (16.7)
Smoker, n (%)	10 (23.8)
Previous covid infection, n (%)	18 (42.9)
Duration from Last known infection (days), (Median, IQR) (n=18)	189.00 (177.00 – 397.25)
Duration from Last Vaccination (days), (Median, IQR)	86.00 (29.25 – 141.00)
Time of vaccination, n (%)	
Morning	18 (42.9 %)
Afternoon	24 (57.1 %)
Anti-Spike Antibody, U/mL (Mean ± SD)	3734.19 ± 2470.43

Table (2) reveals association between anti-Spike antibody level and sex. Female (Mean ± SD) (4857.67 ± 2678.92 U/mL) had higher anti-Spike antibody level than male (Mean ± SD) (4857.67 ± 2678.92 U/mL); however, it was not significantly different [t (40) = -1.566, p = 0.125].

Table (2) Anti-Spike antibody level in both sex (n=42)

Sex	N	Anti-Spike Antibody level (Mean ± SD)	Mean Difference	95 % CI	t value	P value
Male	33	3427.78 ± 2360.83	- 1429.89	- 3275.07 – 415.30	-1.566	0.125
Female	9	4857.67 ± 2678.92				
Independent t test						

Table (3) reveals association between anti-Spike antibody level and BMI status. Anti-Spike antibody level in HCW with various BMI were 3027.21 U/mL in normal BMI group, 5141.42 U/mL in overweight group and 5188.50 U/mL in obese group; increasing antibody level with increasing BMI and it statistically significant (p = 0.028).

Table (3) Anti-Spike antibody level and BMI status (n=42)

BMI	N	Anti-Spike Antibody level (Mean ± SD)	t value	P value
Normal	28	3027.21 ± 2334.90	3.932	0.028
Overweight	12	5141.42 ± 2260.80		
Obese	2	5188.50 ± 2470.43		
One way ANOVA test				

Table (4) shows association between anti-Spike antibody level and presence of diabetes mellitus; strikingly HCW with diabetes mellitus had significantly higher level of anti-Spike antibody level (Median: 6740.00; IQR: 4731.00 – 7500.00 U/mL). Those without diabetes had low level (Median: 2884.00; IQR: 1558.00 – 5000.00 U/mL), (U = 34, p = 0.003).

Table (4) Anti-Spike antibody level and status of diabetes mellitus (n=42)

DM	N	Anti-Spike Antibody level Median (IQR)	t value	Z value	P value
Yes	7	6740.00 (4731.00 – 7500.00)	34	- 2.987	0.003
No	35	2884.00 (1558.00 – 5000.00)			
Mann-Whitney U test					

Anti-Spike antibody level in smokers (Mean ± SD) (3376. 42 ± 2525.69 U/mL) was lower than that of non-smoker (3845.99 ± 2483.05 U/mL); nonetheless, smoking status did not make significant difference [t (40) = 0.520, p = 0.606]. It is shown in Table (5).

Table (5) Anti-Spike antibody level and status of smoking (n=42)

Smoking status	N	Anti-Spike Antibody level (Mean ± SD)	Mean Difference	95 % CI	t value	P value
Smoker	10	3376. 42 ± 2525.69	465.57	-1355.60 –2294.74	0.520	0.606
Non-smoker	32	3845.99 ± 2483.05				
Independent t test						

Table (6) highlights association between anti-Spike antibody level and presence of history of past covid infection. Mean anti-Spike antibody level in HCW with history of covid infection was higher (4013.79 ± 2427.99 U/mL) than that of those without history of covid infection (3524.48 ± 2532.77 U/mL). Nevertheless, it was not statistically significant [t (40) = 0.631, p = 0.532].

Table (6) Anti-Spike antibody level and history of Covid-19 infection status (n=42)

History of Covid	N	Anti-Spike Antibody level (Mean ± SD)	Mean Difference	95 % CI	t value	P value
Yes	18	4013.79 ± 2427.99	489.31	- 1079.08 – 2057.69	0.631	0.532
No	24	3524.48 ± 2532.77				
Independent t test						

Mean anti-Spike antibody level in HCWs who got vaccinated in the afternoon (Mean ± SD) (4350.77 ± 2387.16 U/mL) had higher antibody levels than who got in the morning (2912.07 ± 2933.96 U/mL). However, it was not statistically different [t (40) = -1.929, p = 0.061]. It is demonstrated in Table (7).

Table (7) Anti-Spike antibody level and vaccination injection time of day (n=42)

Injection Time of day	N	Anti-Spike Antibody level Mean ± SD	Mean Difference	95 % CI	t value	P value
Morning	18	2912.07 ± 2933.96	-1438.70	745.95 – -2946.31	-1.929	0.061
Afternoon	24	4350.77 ± 2387.16				
Independent t test						

HCW with history of covid infection in fourth wave (The Omicron) had higher antibody level (Mean ± SD) (4013.79 ± 2427.99 U/mL) than that of those with history of covid infection in third wave (The Delta) (3524.48 ± 2532.77 U/mL).

Table (8) illustrates the independent predictors for anti-Spike antibody level in HCW. The BMI was not significantly different between HCW with diabetes median (IQR): 24.30 (21.00 – 25.54) kg/m2 and those without diabetes: 27.73 (22.03 – 29.38) kg/m2, [U = 75, P = 0.109]. Collinearity statistics was also done for BMI and diabetes status; [tolerance = 0.902 and variant inflation factor = 1.109]. Figure (1) shows correlation between BMI level and anti-Spike antibody level. And, Figure (2) shows association between present of diabetes and anti-Spike antibody level.

Table (8) Independent predictors for anti-Spike antibody level

Predictors	Univariable			Multivariable		
	β	Adjusted R^2	P value	β	Adjusted R^2	P value
Age	79.26	0.059	0.066			
Sex (Female)	1429.89	0.034	0.125			
BMI	216.88	0.130	0.011	149.44	0.248	0.068
Diabetes	3075.55	0.221	0.002	2526.81	0.248	0.010
Smoking	- 469.57	- 0.018	0.606			
History of covid infection	489.31	- 0.015	0.532			
Duration from infection	5.85	0.026	0.247			
Duration from vaccination	- 7.91	0.020	0.181			
Time vaccination	1438.70	0.062	0.061			

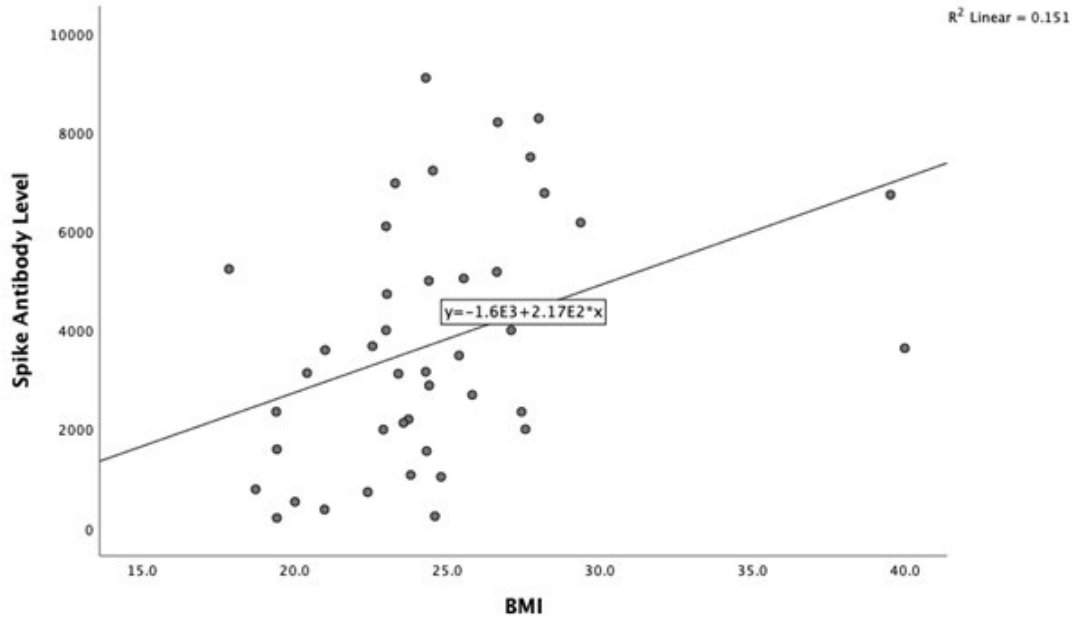


Figure (1) Correlation between BMI and anti-Spike antibody level

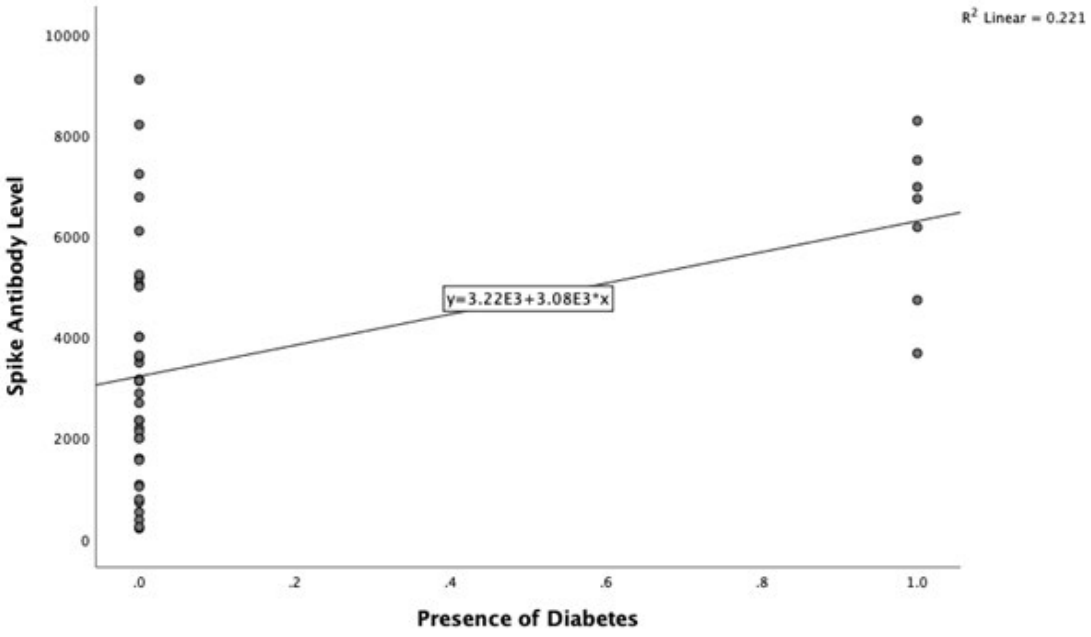


Figure (2) Association between presence of type 2 diabetes and anti-Spike antibody level (0 = Absence of type 2 diabetes, 1 = Presence of type 2 diabetes)

Significant predictors for anti-Spike antibody level on univariable analysis were BMI (β = 216.88, P = 0.011, adjusted R^2 = 0.130) and presence of diabetes (β = 3075.55, P = 0.002, adjusted R^2 = 0.221). The anti-Spike antibody level was not associated with age (β = 79.26, P = 0.066, adjusted R^2 = 0.059), sex (female) (β = 1429.89, P = 0.125, adjusted R^2 = 0.034), smoking status (β = -469.57, P = 0.606, adjusted R^2 = -0.018), history of covid infection (β = 489.31, P = 0.532, adjusted R^2 = -0.015), duration from last vaccination (β = - 7.91, P = 0.181, adjusted R^2 = 0.020) and time of the day of vaccination (afternoon) (β = 1438.70, P = 0.0061, adjusted R^2 = 0.062). In multivariable analysis, only the diabetes status was the significant predictor for anti-Spike antibody level.

Discussion

This descriptive study involved 42 HCW working in acute care hospital (1,000 bedded) in Yangon. The study was done in August 2022, early fifth wave of COVID-19 infection in Myanmar. The mean anti-Spike antibody level of study population was 3734.19 U/mL. Mean anti-Spike protein antibody level of male and female was 3427.78 U/mL and 4857.67 U/mL respectively. Although anti-Spike protein antibody level was higher in female, it was not statistically significant. However, anti-Spike antibody level of female was higher than that of study population 4857.67 U/mL vs 3734.19 U/mL. Therefore, it proved that female had higher antibody positivity following COVID-19 vaccination [17, 26]. Mean age was 40.6 ± 8.9 years as the study was done in working age group. Therefore, the age effect 'older age group had lower antibody response' could not be seen here [17, 26].

There was significant positive relation between BMI and anti-Spike protein antibody level. It overlooked previous reports; obese individual had decrease antibody positivity and higher BMI was associated with lower titers of SARS-CoV-2 spike antibodies in men, but not in women [26, 27, 28, 29]. Following COVID-19 infection, those with high BMI had good antibody response [24, 30]. In this study, anti-Spike antibody level was higher in those with higher BMI; therefore, it confirmed the finding which showed the BMI was positively related with antibody level following vaccination and infection [31]. Further study with larger sample size is needed for this controversial issue.

The HCW with diabetes mellitus in this study had significantly higher level of anti-Spike antibody level (6740.00 U/mL); those without diabetes had low level (2884.00 U/mL). It was higher than the mean anti-Spike antibody level of study population (3734.19 U/mL). Statistically significant higher level of anti-Spike antibody level in HCW with diabetes mellitus neglected previous findings; patients with comorbidity had low antibody response to COVID-19 vaccine [26, 32]. Having high anti-Spike antibody level in HCW with diabetes mellitus might probably related with the mean BMI of HCW with diabetes mellitus. However, there was no significant difference in BMI between HCWs with diabetes and those without diabetes proved by collinearity statistics. Therefore, HCW with diabetes mellitus were having high positive response to COVID-19 vaccine which was not related with BMI status in this study. It pays little attention to previous report that subjects with diabetes mellitus had poor antibody response to COVID-19 vaccine [33].

Anti-Spike antibody levels in smokers (3376.42 U/mL) was lower than that of non-smoker (3845.99 U/mL); nonetheless, smoking status did not make significant difference. It was lower than that study population (3734.19 U/mL). Therefore, confirmed the previous report "smokers were found to have low response to COVID-19 vaccine" [17].

The anti-Spike antibody level in HCWs with history of COVID-19 infection was higher (4013.79 U/mL) than that of those without infection (3524.48 U/mL); nevertheless, it was not significant from statistical point of view. However, it was higher than the mean anti-Anti-Spike antibody level of study population (3734.19 U/mL). Generally, antibody begin to rise within the first few days following an infection with COVID-19 or after the vaccine. Later, the level steadily increases in concentration till 6 months; then, they decline gradually [34]. In this study, time from last COVID-19 infection was 257 days, over 8 months. Therefore, it was not strange that there was no relation between history of known COVID-19 infection and timing from known COVID-19 infection with anti-Spike protein antibody level. In other words, the effect of hybrid immunity was not clearly seen in this study due to time factor [4]. HCW with COVID-19 infection in fourth wave (The Omicron) had higher antibody level (4013.79 U/mL) than that of those in third wave (The Delta) (3524.48 U/mL). In Myanmar, fourth wave (The Omicron) was just 5-6 months before the study i.e., February 2022; and, third wave (The Delta) was 10-12 months ago i.e., August 2021.

Furthermore, negative relation was detected between time from last vaccination to anti-Spike protein antibody level; not statistically significant. However, it provided the evidence to previous findings- antibody response decreased over time particularly after 6 months i.e., waning immunity in all age groups after six months [6]. It demonstrated that the protective efficacy of vaccine decreased with time [34].

Anti-Spike antibody levels in HCWs who got vaccination in the afternoon (4350.77 U/mL) had higher antibody levels than who got in the morning (2912.07 U/mL); not statistically different. However, it was higher than the mean anti-Spike antibody level of study population (3734.19 U/mL). Therefore, it generally confirmed the finding "HCW who received the SARS-CoV-2 vaccine in the afternoon had higher antibody levels than those vaccinated in the morning" [17].

Limitation of the study

Because of low resource setting, there were several limitations. The sample size is not large; future larger studies are required particularly relation between anti-Spike antibody level and BMI and diabetes mellitus. Moreover, serial estimation of anti-Spike antibody level monthly would be helpful to determine exact timing of peak level and lowest level to recommend the best timing for

booster doses. In addition, the study should also include both cellular and humoral responses following vaccination. In this study, 7 different types of vaccine produced from various countries were included. The potency of vaccine in terms of anti-Spike antibody level should be compared with 2 different types of vaccine.

Conclusion

The level of anti-Spike antibody to 3 doses of COVID-19 vaccine in health care workers working in acute care hospital was significantly related with BMI and diabetes mellitus. Those with high BMI and presence of diabetes mellitus had significantly higher level of anti-Spike antibody. Though it was not statistically significant, the anti-Spike antibody level was relatively higher in followings: female; non-smokers; those with COVID-19 infection; those with shorter timing from last infection (The Omicron infection); those with shorter duration from last vaccination; and those who got vaccination in the afternoon.

Acknowledgements

The authors would like to thank all the HCW for giving informed consent to this study. The authors also acknowledged Prof Ko Ko Lwin, Prof Kyaw Zay Ya, Prof Myint Zaw for administrative support, and Professor Tin Moe Mya for laboratory support.

Declaration of conflict of interest

The authors declared no potential conflicts of interests with respect to authorship and publication of this article.

Ethical approval

This study was approved by Hospital Research and Ethic Committee from Defence Services General Hospital (1000-Bedded) Mingaladon, Myanmar. Informed consent was also taken from each HCW.

Funding

The authors received no financial support for publication of this article.

References

1. MOHS. (2021). Coronavirus Disease 2019 (COVID-19) Surveillance Dashboard (Myanmar).
2. Yu, Y., Esposito, D., Kang, Z., Lu, J., Remaley, A. T., De Giorgi, V., ... & Cao, L. (2022). mRNA vaccine-induced antibodies more effective than natural immunity in neutralizing SARS-CoV-2 and its high affinity variants. Scientific reports, 12(1), 1-10.
3. Greaney, A. J., Loes, A. N., Gentles, L. E., Crawford, K. H. D., Starr, T. N., Malone, K. D., Chu, H. Y., & Bloom, J. D. (2021). Antibodies elicited by mRNA-1273 vaccination bind more broadly to the receptor binding domain than do those from SARS-CoV-2 infection. Science Translational Medicine, 13(600).
4. Rodda, L. B., Morawski, P. A., Pruner, K. B., Fahning, M. L., Howard, C. A., Franko, N., Logue, J., Eggenberger, J., Stokes, C., Golez, I., Hale, M., Gale, M., Chu, H. Y., Campbell, D. J., & Pepper, M. (2022). Imprinted SARS-CoV-2-specific memory lymphocytes define hybrid immunity. Cell, 185(9), 1588-1601.e14.
5. Pilz, S., Theiler-Schwetz, V., Trummer, C., Krause, R., & Ioannidis, J. P. A. (2022). SARS-CoV-2 reinfections: Overview of efficacy and duration of natural and hybrid immunity. Environmental Research, 209, 112911.
6. Goldberg, Y., Mandel, M., Bar-On, Y. M., Bodenheimer, O., Freedman, L. S., Ash, N., Alroy-Preis, S., Huppert, A., & Milo, R. (2022). Protection and Waning of Natural and Hybrid Immunity to SARS-CoV-2. New England Journal of Medicine, 386(23), 2201–2212.
7. Hall, V., Foulkes, S., Insalata, F., Kirwan, P., Saei, A., Atti, A., Wellington, E., Khawam, J., Munro, K., Cole, M., Tranquillini, C., Taylor-Kerr, A., Hettiarachchi, N., Calbraith, D., Sajedi, N., Milligan, I., Themistocleous, Y., Corrigan, D., Cromey, L., … Hopkins, S. (2022). Protection against SARS-CoV-2 after Covid-19 Vaccination and Previous Infection. New England Journal of Medicine, 386(13), 1207–1220.
8. Bates, T. A., McBride, S. K., Leier, H. C., Guzman, G., Lyski, Z. L., Schoen, D., Winders, B., Lee, J.-Y., Lee, D. X., Messer, W. B., Curlin, M. E., & Tafesse, F. G. (n.d.). Vaccination before or after SARS-CoV-2 infection leads to robust humoral response and antibodies that effectively neutralize variants. Science Immunology, 7(68), eabn8014.
9. Thiagarajan, K. (2021). What do we know about India's Covaxin vaccine? BMJ, 373, n997.
10. IHME. (2021). COVID-19 vaccine efficacy summary.
11. Ghosh, S., Shankar, S., Chatterjee, K., Chatterjee, K., Yadav, A. K., Pandya, K., Suryam, V., Agrawal, S., Ray, S., Phutane, V., & Datta, R. (2021). COVISHIELD (AZD1222) VaccINe effectiveness among healthcare and frontline Workers of INdian Armed Forces: Interim results of VIN-WIN cohort study. SPECIAL ISSUE: COVID-19 - NAVIGATING THROUGH CHALLENGES, 77, S264–S270.
12. Lopez Bernal, J., Andrews, N., Gower, C., Gallagher, E., Simmons, R., Thelwall, S., Stowe, J., Tessier, E., Groves, N., Dabrera, G., Myers, R., Campbell, C. N. J., Amirthalingam, G., Edmunds, M., Zambon, M., Brown, K. E., Hopkins, S., Chand, M., & Ramsay, M. (2021). Effectiveness of Covid-19 Vaccines against the B.1.617.2 (Delta) Variant. New England Journal of Medicine.
13. UK Health Security Agency, (2021). SARS-CoV-2 variants of concern and variants under investigation in England.
14. CDC. (2022). Vaccine Effectiveness & Breakthrough Surveillance.
15. Andrews, N., Stowe, J., Kirsebom, F., Toffa, S., Rickeard, T., Gallagher, E., Gower, C., Kall, M., Groves, N., O'Connell, A.-M., Simons, D., Blomquist, P. B., Zaidi, A., Nash, S., Iwani Binti Abdul Aziz, N., Thelwall, S., Dabrera, G., Myers, R., Amirthalingam, G., … Lopez Bernal, J. (2022). Covid-19 Vaccine Effectiveness against the Omicron (B.1.1.529) Variant. The New England Journal of Medicine, 386(16), 1532–

1546.
16. Nobis, C. C., Dubeau Laramée, G., Kervezee, L., Maurice De Sousa, D., Labrecque, N., & Cermakian, N. (2019). The circadian clock of CD8 T cells modulates their early response to vaccination and the rhythmicity of related signaling pathways. Proceedings of the National Academy of Sciences, 116(40), 20077–20086.
17. Wang, L., Li, J., Gao, Y., Li, R., Zhang, J., Su, D., Wang, T., Yang, G., & Wang, X. (2019). Association between coronary dominance and acute inferior myocardial infarction: A matched, case-control study. BMC Cardiovascular Disorders, 19(1), 35.
18. Sabetian, G., Moghadami, M., Hashemizadeh Fard Haghighi, L., Shahriarirad, R., Fallahi, M. J., Asmarian, N., & Moeini, Y. S. (2021). COVID-19 infection among healthcare workers: A cross-sectional study in southwest Iran. Virology Journal, 18(1), 58.
19. Tyagi, K., Ghosh, A., Nair, D., Dutta, K., Singh Bhandari, P., Ahmed Ansari, I., & Misra, A. (2021). Breakthrough COVID19 infections after vaccinations in healthcare and other workers in a chronic care medical facility in New Delhi, India. Diabetes & Metabolic Syndrome: Clinical Research & Reviews, 15(3), 1007–1008.
20. Al-Kuwari, M. G., AbdulMalik, M. A., Al-Nuaimi, A. A., Abdulmajeed, J., Al-Romaihi, H. E., Semaan, S., & Kandy, M. (2021). Epidemiology Characteristics of COVID-19 Infection Amongst Primary Health Care Workers in Qatar: March-October 2020. Frontiers in Public Health, 9, 570.
21. Barranco, R., & Ventura, F. (2020). Covid-19 and infection in health-care workers: An emerging problem. Medico-Legal Journal, 88(2), 65–66.
22. Sharma, P., Mishra, S., Basu, S., Tanwar, N., & Kumar, R. (2021). Breakthrough infection with SARS-CoV-2 and its predictors among healthcare workers in a medical college and hospital complex in Delhi, India. MedRxiv, 2021.06.07.21258447.
23. Niyas, V. K. M., & Arjun, R. (2021). Response to letter re Breakthrough COVID-19 infections among health care workers after two doses of ChAdOx1 nCoV-19 vaccine. QJM : Monthly Journal of the Association of Physicians.
24. Pyar, K. P., Hla, S., Min, A., Wunn, D., Aung, Z. N., Lin, M., Win, T., Aung, L., Kyaw, A., Ya, K., Tun, T., Kyaw, M., Oo, Z., Aung, Z., Lin, T., & Htun, S. (2021). Breakthrough Infection among Fully Vaccinated Physicians Working in COVID-19 Treatment Centers; Prevalence, Presenting Symptoms, Co-Morbidities and Outcome in the Third Wave of Epidemics in Myanmar. Journal of Biomedical Research & Environmental Sciences, 2, 721–730.
25. Pyar, K. P. (2022). Breakthrough infections due to SARS-CoV-2 Wild type, the Delta variant and the Omicron variant in early fourth wave of epidemics in Myanmar. International Journal Of Medical Science And Clinical Research Studies, 02(02).
26. Ward, H., Whitaker, M., Flower, B., Tang, S. N., Atchison, C., Darzi, A., Donnelly, C. A., Cann, A., Diggle, P. J., Ashby, D., Riley, S., Barclay, W. S., Elliott, P., & Cooke, G. S. (2022). Population antibody responses following COVID-19 vaccination in 212,102 individuals. Nature Communications, 13(1), 907.
27. Malavazos, A. E., Basilico, S., Iacobellis, G., Milani, V., Cardani, R., Boniardi, F., Dubini, C., Prandoni, I., Capitanio, G., Renna, L. V., Boveri, S., Carrara, M., Spuria, G., Cuppone, T., D'acquisto, A., Carpinelli, L., Sacchi, M., Morricone, L., Secchi, F., … Corsi Romanelli, M. M. (2021). Antibody responses to BNT162b2 mRNA vaccine: Infection-naïve individuals with abdominal obesity warrant attention. MedRxiv, 2021.09.10.21262710.
28. Yamamoto, S., Mizoue, T., Tanaka, A., Oshiro, Y., Inamura, N., Konishi, M., Ozeki, M., Miyo, K., Sugiura, W., Sugiyama, H., & Ohmagari, N. (2022). Sex-associated differences between BMI and SARS-CoV-2 antibody titers following the BNT162b2 vaccine. Obesity (Silver Spring, Md.), 30(5), 999–1003.
29. Kara, Z., Akçin, R., Demir, A. N., Dinç, H. Ö., Taşkın, H. E., Kocazeybek, B., & Yumuk, V. D. (2022). Antibody Response to SARS-CoV-2 Vaccines in People with Severe Obesity. Obesity Surgery, 32(9), 2987–2993.
30. Zhai, B., Clarke, K., Bauer, D. L., Moehling Geffel, K. K., Kupul, S., Schratz, L. J., Nowalk, M. P., McElroy, A. K., McLachlan, J. B., Zimmerman, R. K., & Alcorn, J. F. (2022). SARS-CoV-2 Antibody Response Is Associated with Age and Body Mass Index in Convalescent Outpatients. The Journal of Immunology, ji2101156.
31. Lombardi, A., Consonni, D., Oggioni, M., Bono, P., Uceda Renteria, S., Piatti, A., Pesatori, A. C., Castaldi, S., Muscatello, A., Riboldi, L., Ceriotti, F., Bandera, A., & Gori, A. (2021). SARS-CoV-2 anti-spike antibody titres after vaccination with BNT162b2 in naïve and previously infected individuals. Journal of Infection and Public Health, 14(8), 1120–1122.
32. Rangsrisaeneepitak, V., Porntharukchareon, T., Dechates, B., Sirisreetreerux, S., & Tawinprai, K. (2022). Antibody levels in people with diabetes after one dose of the ChAdOx1 nCoV-19 (AZD1222) vaccine. Diabetology International.
33. Soetedjo, N. N. M., Iryaningrum, M. R., Lawrensia, S., & Permana, H. (2022). Antibody response following SARS-CoV-2 vaccination among patients with type 2 diabetes mellitus: A systematic review. Diabetes & Metabolic Syndrome, 16(2), 102406.
34. Ortega, N., Ribes, M., Vidal, M., Rubio, R., Aguilar, R., Williams, S., Barrios, D., Alonso, S., Hernández-Luis, P., Mitchell, R. A., Jairoce, C., Cruz, A., Jimenez, A., Santano, R., Méndez, S., Lamoglia, M., Rosell, N., Llupià, A., Puyol, L., … Dobaño, C. (2021). Seven-month kinetics of SARS-CoV-2 antibodies and role of pre-existing antibodies to human coronaviruses. Nature Communications, 12(1), 4740.