Original Research Article

To boost or not? Serum anti-COVID IgG in double vaccinated MBBS students: a cross-sectional study

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ABSTRACT

Background: Aim of the study was to estimate the prevalence of sero-positivity i.e. serum anti-covid IgG >1.4 AU/ml in MBBS students of our Institute.
Methods: This study was carried out on 75 MBBS students of our institute (10% of 750 MBBS students of Amaltas institute of Medical Sciences Dewas M.P. India) during period of August 2022 to November 2022. All serum anti-covid IgG titres above 1.4 AU/ml were considered sero-positive and the prevalence of sero-positivity was calculated. MBBS students were asked to fill out a questionnaire regarding their clinical history of testing positive for covid, exposure to COVID-19 patients, their covid appropriate behavior, etc. After obtaining informed consent, 4 ml venous blood samples were collected for determining serum anti-covid IgG titre on Chemiluminescence analyzer. 75 MBBS students divided into 2 groups – those who completed between 6-9 months and those who have completed more than 9 months after the 2nd dose of vaccine. The mean serum anti-covid IgG titre was compared.
Results: The prevalence of sero-positivity was 94.66% calculated in MBBS students of our institute. The total antibody sero-positivity was higher in males (98.11%) than in females (86.36). The duration after 2nd dose of vaccine; over the time 6-9 months serum anti-covid IgG titre significantly high but after more than 9 months serum anti covid IgG titre significantly decline (p<0.001) and significant correlation was found between duration after 2nd dose of vaccine and serum anti-covid IgG titres (p<0.001).
Conclusions: This study; strongly recommended the need for booster doses for long-duration protection against COVID-19 re-infection and its emerging new variants.

Keywords: Booster doses, COVID-19 Pandemic, Prevalence, Sero-positive, Severe Acute Respiratory Syndrome Corona virus 2, WHO

INTRODUCTION

The corona virus disease 2019 (COVID-19) pandemic is believed to have started in Wuhan, Hubei, China in November 2019, from where it spread worldwide.[1] First case of COVID-19 infection was reported in India from Kerala.[2] India started COVID-19 vaccination in the country from 16th January 2021. About 200 crores vaccine doses have been administered till now, with 94.9 crore being fully vaccinated with two doses.[3]

Antibody titres after two doses of vaccine have been reported to decline after 3 months.[4] However, lower but adequate titres of protective antibody have been claimed for 6 to 9 months after 2nd dose of vaccine.[5,6] Since the omicron variant in the third wave is highly infectious and vaccine efficacy after 9 months is doubtful, India started administering the precaution or third dose of vaccine from 10th January, 2022. The third dose has been reported to be effective in providing protection against the omicron variant, but this is being administered to only its vulnerable population of senior citizens and healthcare workers.[7]

In November 2021, 178 students of SDM College of Medical Sciences at Karnataka's Dharwas and 54 students of Veer Surendra Sai Institute of Medical Sciences at Orissa's Vimsar tested positive. One student of our institute expired last year after contracting COVID-19. Medical students thus can also be considered as a vulnerable population. However, they are not involved in clinical practice against COVID-19. But they attend lectures in groups in enclosed classes, which are often air conditioned and without ventilation, many students live in cluster in hostel. Students have exposure to hospital environment as a part of their clinical teaching or clinical rotations, students may come in contact individuals infected with this disease, such as healthcare workers. A high level of acceptance of vaccination is needed for medical students to protect their health and the health of patients from COVID-19.[8]

Sero-prevalence over the time is the main indicator of the maintenance of specific antibodies against COVID-19.[9] studies reported that quantitative IgM and IgG assays play an important role in the diagnosis of COVID-19.[10] The higher Sensitivity of IgG level plays an important role as a diagnostic tool for ruling out the possibility of COVID-19.[11]Somestudiesreported to be necessary to elucidate the duration of anti-SARS-CoV-2 antibodies, as well as the correlation between seropositivity and protective immunity against reinfection.[12]

Vaccination for those above the age of 18 years started in July, 2021, so most of these students have completed six months after vaccination. Necessity of a precaution dose of vaccine for them would depend on their level of protective antibody; Most of the medical student in our institute completed the second dose of the COVID-19 vaccine and vaccine efficacy after 9 months is doubtful, also, there is most important to know adequate serum anti-COVID IgG titre for MBBS students of our institute. Almost all academics session were started offline studies, also in medical colleges, medical learning cannot take place without clinical postings, and during their clinical posting or rotation, it is important to know if clusters of medical students have adequate protective antibodies. Lower seropositivity prevalence is highly recommended, for a precautionary dose of vaccine in medical students.

METHODS

Sample size

Stratified random sampling (15 students were randomly selected from each of the five batches of 150 students using random numbers from random.org).

Study place

The study was carried out on 75 MBBS students of Amaltas institute of Medical Sciences (10% of 750 MBBS students of our Institute).

Study duration

The duration of the study was from August 2022 to November 2022 on 75 MBBS students for ICMR- STS-2022.This report STS-2022 awarded from A-grade which is interpreted as outstanding performance.

Inclusion criteria

All double vaccinated MBBS students of Amaltas institute of Medical Sciences who have completed 6 months after vaccination.

Exclusion criteria

Ethical consideration with required forms: Permission from the Amaltas institute of Medical Sciences, Institutional Ethics Committee was taken prior to commencing the study. Informed consent of participants was taken.

Data collection procedure & instruments

MBBS students were asked to fill out a proforma and questionnaire (here attached format) regarding their clinical history of testing positive for COVID, exposure to COVID-19 patients, their COVID appropriate behavior, etc which prepared by available knowledge of pandemic.

After obtaining informed consent, a 4 ml venous blood sample were collected for measuring serum anti-COVID IgG using Vector Biotech Kits (Specificity: 97.33% and Sensitivity: 91.21%) on Maglumi 800 Chemiluminescence analyzer.

Quality control

Vector Biotech kits come with calibrators and control. Validation of calibration and control result was done before processing samples.

Confidentiality

Individual test report was disclosed only to participant; they will not be published or disclosed to others.

Plan of analysis/ statistical analysis

All serum anti-COVID IgG titres above 1.4 AU/ml considered as seropositive 13 and prevalence of seropositivity calculated. 75 MBBS students divided into 2 groups – those who completed between 6-9 months and those who have completed more than 9 months after the 2nd dose of vaccine. The mean serum anti-COVID IgG titre compared using student t-test. Distribution of any comorbidities, personal habits, COVID appropriate behavior, history of testing positive for COVID-19 or exposure to COVID patients were seen across the groups. Value of correlation coefficient and statistical

significance of the correlation of serum anti-COVID IgG titre with duration after 2nd dose of vaccine were also be seen. Statistical analysis was carried out using IBM SPSS Version.[16] The mean serum anti-COVID IgG compared using the student t-test of association was applied at a 5% level of significance.

RESULTS

75 MBBS students participated in this study. Their mean characteristics were as follows: age 22.68±2.00 from 19-27 years, serum anti-COVID IgG titres were 248.73±155.02 from 0.248-526 AU/ml. Serum anti-COVID IgG titres above 1.4 AU/ml are considered seropositive (20) out of 75 only 4 students were found Sero-negative their Serum anti COVID IgG titre value below 1.4 AU/ml and the prevalence of seropositivity was 94.66% calculated in MBBS students of our institute.

Table 1 shows the prevalence of seropositivity with serum anti COVID IgG titre. Out of 75 MBBS students in the study participants, 22/75 (29.33%) were females, and 52/75 (70.66%) were males. Out of 22 females, 19 females were Sero-positive and 3 females were sero-negative while out of 52 males only 01 male was sero-negative. The prevalence of Seropositivity in females was 86.36% (N-19/22) while in males was 98.11% (N-01/51). In males prevalence of seropositivity was higher than in females. The Serum anti COVID IgG titre in females and males were 250.87 ± 162.70 AU/ml and 247.86 ± 153.33 respectively. The difference is bound to be insignificant.

Table 2 show the Prevalence of Seropositivity as per Prof. /Year of MBBS with Serum anti COVID IgG titre. Stratified random sampling, 15 students were randomly selected from each of the five batches of 150 students. Out of five batches, batch-2017 was found 100 =% Prevalence of seropositivity while all four batches Batch-21, Batch-20, Batch-2019, and Batch-2016 were the same prevalence of Seropositivity at 93.33% each. The Serum anti COVID IgG titre in Batch-2021, Batch-2020, Batch-2019, Batch-2017 and Batch-2016 were 315.29±164.49 AU/ml, 185.27 ±128.68 AU/ml, 292.85±163.05 AU/ml, 269.35±151.53 AU/ml and 180.95±131.76 AU/ml respectively. Serum anti-COVID IgG titre was significantly lower in Batch-2016 while higher in Batch - 2021.

Table 3 shows the distribution of student characteristics with Serum anti COVID IgG titre. In terms of percentage, 29.33% (N-22) were female and 70.66% (N-53) were male their Serum anti COVID IgG titre was 250.87±162.70 AU/ml and 247.86±153.34 AU/ml respectively. The two-tailed P value equals 0.94. The difference is bound to be insignificant. 68% of students stayed in hostel in groups and shared rooms only 09.33% stay in outside. The Serum anti COVID IgG titre hostel and outside stayed students were 251.27±154.89 AU/ml and 224.23±166.62 AU/ml respectively. The two-tailed Pvalue equals 0.66. The difference is bound to be

insignificant. 82.66 % (N-62) students there is no H/O COVID test Positive (RTPCR) while 17.33% (N-13) have H/O COVID test (RTPCR) Positive and their Serum anti-COVID IgG titre was 278.86±141.14 AU/ml and 242.43±158.13 AU/ml respectively. The two-tailed P value equals 0.44. The difference is bound to be insignificant. 29.33% (N-22) students reported to H/O COVID like Symptoms (fever-45%(N-10), Cough-31.81% (N-07), Breathlessness-13.63% (N-03), Loss of smell-13.63 (N-03), Diarrhea-00%, Body ache- 36.36% (N-08), and 22.72% (N-05) not specified their symptom but they accepted to COVID like symptoms). And 70.66% (N-53) there is no H/O COVID like symptoms their Serum anti COVID IgG titre was 282.97±143.99 AU/ml and 234.53±158.53 AU/ml respectively. The two-tailed P value equals 0.22. The difference is bound to be insignificant. 29.33% (N-22) students reported H/O. Contact with the COVID positive person and 70.66% (N-53) there is no H/O contact with the COVID positive person their Serum anti COVID IgG titre was 248.48±145.68 AU/ml and 248.85±160.11 AU/ml respectively.

The two-tailed Pvalue equals 0.99. The difference is bound to be insignificant. 04% (N=03) students reported H/O death in their family due to COVID and 96% (N=72) there is no H/O death in their family due to COVID Contact their Serum anti COVID IgG titre was 373.03±95.73 AU/ml and 243.56±155.28 AU/ml respectively. The two-tailed Pvalue equals 0.15. The difference is bound to be insignificant. There is no H/O Foreign travel reported by any students in this study. 28% (N=21) students reported H/O attending gatherings and 72% (N-54) there is no H/O attending gathering their Serum anti COVID IgG titre was 279.45±161.87 AU/ml and 236.79±152.16 AU/ml respectively. The two-tailed p value equals 0.28. The difference is bound to be insignificant. The serum anti-COVID IgG titre compared with COVID-related safety behavior like rate use of sanitizer/handwash (Pvalue 0.30), Rate use of mask (p value 0.39) and type of mask used usually (p value 0.45). The mean serum anti-COVID IgG titre compared using ANOVA between the groups and within the groups, there is no significant change observed in the serum anti-COVID IgG titre compared using ANOVA between the groups and within the groups, there is no significant change observed in the serum anti-COVID IgG titre. 98.66% (N=74) students reported there is no comorbidity and 01.33% (N=01) students reported comorbidity but not specified by his/her. Like diabetes, hypertension and other-specify. 86.66% (N=62) students, preferred to take a precautionary dose if offered while 17.33% (N=13) students were not preferred to take a precautionary dose if offered their serum anti-COVID IgG titre was 245.24±150.57 AU/ml and 265.43±180.57 AU/ml respectively.

The two-tailed p value equals 0.67. The difference is bound to be insignificant. There is no significant change in the Serum anti COVID IgG titre.98.66% (N=74)

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Table 1: Prevalence of seropositivity with serum anti-COVID IgG titre.

Gender	Number	Sero-Positive	Sero-Negative	Prevalence of Seropositivity	Serum anti-COVID IgG titre (Mean±SD) (AU/ml)
Female	22 (29.33%)	19	3	86.36%	250.87±162.70
Male	53 (70.66%)	52	1	98.11%	247.86±153.33
Overall	75 (100%)	71	4	94.66%	248.73±155.02

Table 2: Prevalence of seropositivity according to their prof./year of MBBS students with serum anti-COVID IgG titre.

Prof./Year of MBBS	Number	Sero-Positive	Sero-Negative	Prevalence of Sero-Positivity	Serum anti-COVID IgG titre (Mean±SD) (AU/ml)
Batch-2021	15	14	1	93.33%	315.29±164.49
Batch-2020	15	14	1	93.33%	185.27±128.68
Batch-2019	15	14	1	93.33%	292.85±163.05
Batch-2017	15	15	0	100%	269.35±151.53
Batch-2016	15	14	1	93.33%	180.95±131.76
Overall	75	71	4	94.66%	248.73±155.02

Table 3: Distribution of the student characteristics with serum IgG titre.

Characteristic	Category		Number (%)	Serum anti-COVID IgG titre (Mean±SD) (AU/ml)	P value
Gender	Female		22 (29.33)	250.87±162.70	0.94 (NS)
	Male		53 (70.66)	247.86±153.34	
Staying In	Hostel		68 (90.66)	251.27±154.89	0.66 (NS)
	Outside		07 (09.33)	224.23±166.62	
H/O COVID test positive (RTPCR)	Yes		13 (17.33)	278.86±141.14	0.44 (NS)
	No		62 (82.66)	242.43±158.13	
H/O COVID like symptoms	Yes		22 (29.33)	282.97±143.99	0.22 (NS)
	1.	Fever	10 (45.45)		
	2.	Cough	07 (31.81)		
	3.	Breathlessness	03 (13.63)		
	4.	Loss of smell	03 (13.63)		
	5.	Diarrhea	00		
	6.	Body ache	08 (36.36)		
	7.	Not specified	05 (22.72)		
	No		53 (70.66)	234.53±158.53	
H/O Contact with COVID positive person	Yes		22 (29.33)	248.48±145.68	0.99 (NS)
	No		53 (70.66)	248.85±160.11	
H/O Death in family due to COVID	Yes		03 (04)	373.03±95.73	0.15 (NS)
	No		72 (96)	243.56±155.29	
H/O Foreign travel	Yes		00 (00)	00.00±00.00	NA
	No		75 (100)	248.74±155.04	
H/O attending gathering	Yes		21 (28)	279.49±161.87	0.28 (NS)
	No		54 (72)	236.79±152.16	

Continued.

Characteristic	Category	Number (%)	Serum anti-COVID IgG titre (Mean±SD) (AU/ml)	P value
Rate use of sanitizer/Hand wash	No use	02 (2.6)	446.75±39.24	0.30 (NS)
	Rarely	03 (4)	292.68±253.46	
	Occasionally	21 (28)	217.55±134.66	
	Frequently	35 (46.66)	261.65±153.42	
	Very Frequently	14 (18.66)	225.57±168.19	
Rate use of mask	No use	02 (2.6)	446.75±39.24	0.39 (NS)
	Rarely	03 (4)	184.33±53.35	
	Occasionally	28 (37.33)	255.12±167.16	
	Frequently	18 (24)	250.44±156.31	
	Very Frequently	24 (32)	231.59±147.83	
Type of mask used usually	Cloth	05 (6.66)	248.32±138.60	0.45 (NS)
	Surgical	37 (49.33)	265.05±162.65	
	N-95	27 (36)	255.82±153.410	
	Cloth+N-95	01 (01.33)		
	Surgical+N95	01 (01.33)		
	Surgical+ Cloth	04 (05.33)	120.67±83.38	
Any Co morbidity	Yes	01 (01.33)		NA
	No	74 (98.66)	246.54±154.91	
Prefer to take a pre-caution dose if offered	Yes	62 (86.66)	245.24±150.57	0.67 (NS)
	No	13 (17.33)	265.43±180.57	

95% Confidence Interval, 5% level of significance (p<0.05). NS-non-significant.

Table 4: Association of serum IgG titre with duration after 2nd dose of vaccine.

Duration after 2nd dose of Vaccine	Number (%)	Serum anti COVID IgG titre (AU/ml)	P value (Significance)
6-9 months	23 (30.66%)	361.54±133.77	0.000 (Extremely Statistically Significance)
>9 months	52 (69.33%)	198.85±137.41	

99% Confidence Interval, 1% level of significance (p<0.001)

Table 5: Association of serum anti-COVID IgG titre with administered vaccine

Name of vaccine	Number (%)	Serum anti-COVID IgG titre (AU/ml)	P value (Significance)
Covisheld	57 (76)	270.01±153.63	0.009 (Extremely Statistically Significance)
Covaxin	16 (21.33)	153.61±125.93	
Sputnik-V	2 (02.66)	403.66±24.66	
Total	75 (100)	248.74±155.04	

95% Confidence Interval, 5% level of significance (p<0).

Table 6: Correlation of serum anti-COVID IgG with duration after 2nd dose of vaccine.

Correlation	Number	Serum anti-COVID IgG titre (Mean±SD) (AU/ml)	Pearson Correlation (r)	P value (2-tailed)
Serum anti COVID IgG titre	75	248.74 ±155.04	-.470**	0.000 (Extremely Statistically Significant)
Duration after 2nd dose of vaccine	75	11.90 ± 2.77		

Correlation is significant at the 0.01 level (2-tailed).

Table 4 show a significant Association of Serum IgG titre with Duration after 2nd dose of the Vaccine. 30.66% (N-23) students completed between 6-9 months and 69.33% (N=52) who were completed more than 9 months after the 2nd dose of vaccine. Their Serum anti-COVID IgG titre was 361.54±133.77 AU/ml and 198.85±137.41 AU/ml respectively. The increased serum anti-COVID IgG titre in those who were completed between 6-9 months is to be extremely statistically significant (p<0.000).

Table 5 show a significant Association of Serum IgG titre with the type of Vaccine. 76% (N-57) students were reported to administered Covishield, 21.33% (N-16) were reported to administer Covaxin and only 02.66% (N-02) were reported to administer Sputnik-V, COVID-19 vaccine. Their Serum anti-COVID IgG titre was 270.01±153.63 AU/ml, 153.61±125.93 AU/ml, and 403.66±24.66 AU/ml respectively. The serum anti-COVID IgG titre compared using ANOVA between the groups and within the groups, there is to be extremely statistically significant (p<0.009).

Table 6 show a significant correlation of serum anti-COVID IgG with duration after 2nd dose of vaccine. The Serum anti-COVID IgG titre was 248.74 ±155.04 (AU/ml) and the duration after 2nd dose of the vaccine were 11.90 ± 2.77 months. Their Pearson Correlation (r) value r= -0.470 lies between 0.3-07. The correlation is to be moderate, negative relationship and significant (p<0.000) at the 0.01 level (2-tailed).

DISCUSSION

Several studies reported knowing whether COVID-19 vaccine effectiveness wanes are crucial for informing vaccine policy, such as the need for and timing of booster doses. In our study, overall sero-prevalence was 94.66% (71/75) calculated in MBBS students of our institute duration after 2nd dose of the vaccine. It is a higher sero-prevalence compared to an earlier report by medical students at the University of Copenhagen.[14] A study reported that in males 98.11% (52/53) Sero-prevalence was higher than in female 86.36% (19/22). Wajiha Javed et al also reported that total antibody sero-positivity was higher in males than females.[15] Several factors like close unprotected contact with COVID positive person, traveling history, any comorbidities, personal habits, COVID appropriate behavior are associated with increased COVID-19 antibody seropositivity.

Our study reported that 100% (15/15) Sero-prevalence in Batch-2017 (Final year) and other batches 1st prof, 2nd prof, pre-final, and interns were 93.33% (14/15) each sero-prevalence reported after 2nd dose of vaccines. It could be due to small and specific population-based studies. But most imported here higher sero-prevalence reported in every batch which shows to higher efficacy of vaccine and immunity against the COVID-19. Our study reported that the Serum anti COVID IgG titre with gender there is to be insignificant. The study also reported that staying hostel and outside students, their serum anti COVID IgG titre, did not observe any significant change. The study also reported that when comparing the serum anti COVID IgG titre with a history of COVID test positive and those who have not COVID test positive, there is to be insignificant. In this study, 22 (29.33%) reported H/O COVID like symptoms. 45.45% (10/22) reported fever, 36.36% (08/22) reported body ache, 31.81% (07/22) reported Cough, 13.63% (03+3/22) reported Breathlessness and loss of smell, and 22.72%

(05/22) not reported any symptoms. Most students reported fever and when comparing Serum anti COVID IgG titre with H/O COVID-like symptoms and those who have not H/O COVID-like symptoms, there is to be insignificant. Our study reported that the serum anti COVID IgG titre compared with H/O contact with COVID positive person. Death in family due to COVID, foreign travel and those who have not H/O contact with COVID positive person, Death in family due to COVID, foreign travel, there is to be insignificant. The study also reported that Serum anti COVID IgG titre with personal habits, COVID appropriate behavior like rate use of sanitizer/hand wash, rate use of mask, Type of mask used usually, compared using ANOVA between the groups and within the groups, there is no significant change observed in the serum anti-COVID IgG titre. In our study 98.66% (N-74) students reported there is no comorbidity and 01.33% (N-01) students reported comorbidity but not specified by His/Her. Like-Diabetes, Hypertension, and other-specify. The study also reported that our result Serum anti COVID IgG titre does not associate with any comorbidity.

Most of the medical students in our institute completed the second dose of the COVID-19 vaccine and they were willing to receive a third dose. Confidence in vaccines, relaxation of mobility restrictions, and concern about the sustainability of immunity motivated willingness to receive the third dose of the COVID-19 vaccine in medical students.[8] Our study also reported that the majority of students 76% (57/75) administered covishield which was also administered by the majority of the Indian population, 21.33% (16/75) administered Covaxin, and only 2.66% (02/75) administered sputnik-V. The study also reported the serum anti-COVID IgG titre compared between the groups and within the groups, there is to be an extremely statistically significant value (p<0.009). There are several factors associated with this like, kind of vaccine, manufacturing process, duration of administering doses and personal habits, COVID appropriate behavior, etc. There is a need for more study to explore this area. Our study most importantly reported first duration after 2nd dose of vaccine over the time after 6-9 months, Serum anti COVID IgG titre significantly high after more than 9 months, Serum anti-COVID IgG titre significantly declines. The study also observed a significant correlation between serum anti-COVID IgG titre (248.74±155.04 AU/ml) and Duration after 2nd dose of vaccine (11.90±2.77 AU/ml). Their Pearson Correlation value (r)=–0.470 lies between 0.3-07. The correlation was serum anti-COVID IgG titre and duration after 2nd dose, is to be moderate, negative relationship and significance (p value<0.001) at the 0.01 level (2-tailed). Our study clearly states that as the duration after 2nd dose of vaccine increases the Serum anti COVID IgG titre will be decreased. Protection against the COVID-19 and its emerging new variant needs to maintain a higher Serum anti COVID IgG titre which is easily obtained from taking booster doses of COVID-19 vaccine.

CONCLUSION

The overall sero-positivity of COVID-19 antibodies in MBBS students of our institute was very high (94.66%). The total antibody seropositivity was higher in males (98.11%) than in females (86.36). Our study first provides useful information about duration after 2nd dose of vaccine; over the time 6-9 months serum anti-COVID IgG titre significantly high but after more than 9 months serum anti COVID IgG titre significantly declines. There is inverse correlation between the time interval after 2nd dose of vaccine and Serum anti COVID IgG titre, as with the duration of time serum anti-COVID IgG titre declines. Protection against the COVID-19 and its emerging new variant needs to maintain a higher Serum anti COVID IgG titre which is easily obtained from taking booster doses of COVID-19 vaccine. Hence need for a booster dose of COVID vaccine in MBBS students of our institute.

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