

# Duration of immunity against COVID-19 after vaccination in Indian subcontinent

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## Research Article

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# Abstract

Coronavirus disease (COVID-19) continues to be a major health concern leading to substantial mortality and morbidity across the world. Vaccination is effective in reducing the severity and associated mortality. Data pertaining to the duration of immunity, antibody waning and the optimal timing of booster dose administration is limited. In this cross-sectional study, we assessed the antibody levels in healthcare workers who were fully vaccinated after obtaining Institutional ethics committee approval and informed consent. Whole blood was collected and enumeration of S1/S2 neutralizing antibody levels was carried out using LIAISON SARS-CoV-2 S1/S2 IgG assay. A total of 1636 individuals who were vaccinated with Covaxin or Covishield were included. Of these, 52% were males with a median age of 29 years. Diabetes and Hypertension was noted in 2.32% (38/1636) and 2.87% (47/1636) of the individuals. Spike neutralizing antibodies were below the detectable range (<15 AU/ml) in 6.0% (98/1636) of the individuals. Decline in neutralizing antibody was seen in 30% of the individuals above 40 years of age with comorbidities (diabetes and hypertension) after 6 months. These individuals may be prioritized for a booster dose at 6 months.

## Introduction:

COVID-19 (Coronavirus disease) pandemic continues to be a major public health concern worldwide. Vaccination is currently the only effective option to minimize the burden of disease and reduce mortality.<sup>1</sup> Although healthcare and frontline workers were vaccinated on priority almost a year earlier, data pertaining to duration of immunity, waning of antibodies and the timing of booster doses thereof is limited from India. We therefore assessed the antibody levels in individuals who were fully vaccinated either with Covishield or Covaxin.

## Methods:

**Participant recruitment:** This cross-sectional study was carried out at AIG Hospitals which is a tertiary care centre located at Hyderabad, India after obtaining approval from Institutional ethics committee of AIG hospitals. Fully vaccinated individuals from all the departments of the hospital that included Clinicians, Residents, Nurses, Laboratory personnel, Research Scientists, Security staff, Transport personnel and who provided consent were included in the study. Clinical and demographic details of all the individuals along with vaccination date and type were recorded. Individuals who received only single dose of either Covishield, Covaxin, Sputnik or Pfizer were excluded from the study. Whole blood (3 ml) was collected and anti-spike antibody levels were assessed irrespective of the time from the 2nd dose of vaccination.

**Enumeration of S1/S2 neutralizing antibody levels:** Spike neutralizing antibodies were enumerated employing LIAISON SARS-CoV-2 S1/S2 IgG assay<sup>2</sup> which is a chemiluminescence immunoassay (CLIA) for the quantitative detection of IgG anti-S1 and IgG anti-S2 antibodies to SARS-CoV-2. The quantification range is between 3.8 and 400.0 AU/mL. Intra and inter-assay precision of the kit ranges between 0 and

4%. The specificity is 98.5% (97.5-99.2) and sensitivity is 97.4% >15 days after diagnosis at a cut-off of >15 AU/mL according to the manufacturer. Results were calculated and the antibody concentrations were expressed as arbitrary units (AU/mL). Concentrations of <15.0 AU/mL were interpreted as negative and  $\geq 15.0$  AU/mL as positive. 100 AU/mL was considered as protective immunity based on our in-house data on breakthrough infections.

## Statistical analysis:

Statistical analysis was performed using SPSS ver. 25. Continuous variables were expressed as median (range) or mean (standard deviation) and compared using Student's t-test while the categorical variables were expressed as n (%) and compared using Chi-square test.

## Results:

A total of 1636 individuals consented to participate in the study. Of these, 52% were males with a median age of 29 (18-79) years. Approximately 3% of the individuals had diabetes mellitus (38/1636) and hypertension (47/1636). Of the 1636, 93% (1519/1636) received Covishield, 6.2% received Covaxin (n= 102), and <1% received sputnik (n= 13) & Pfizer vaccine (n= 2). Approximately 12% (208/1636) had prior history of COVID-19 infection.

S1/S2 spike neutralizing antibodies were below the detectable range (Negative) in 98/1636 (6.0%) of the individuals at 6 months post 2nd dose of vaccination. Of the 98 who did not have antibodies, 57.14% (56/98) were males and remaining were females (42/98; 42.86%) and the difference was not statistically significant (P=0.29). There was a significant (P=0.05) increase in the number of individuals with negative antibody levels at 6 months as compared to beyond 6 months (12/325; 3.7% Vs. 86/1311; 6.6%; Figure 1). Likewise, a similar increase of individuals with antibody titres <100 AU/mL was seen at 6 months as compared to beyond 6 months (68/325; 21.0% Vs. 409/1311; 31.2%), and the difference was statistically significant (P<0.001; Figure 2).

Comparison of individuals with negative S1/S2 spike neutralizing antibodies (below the detectable range) based on age revealed a significant (P=0.007) increase in the number with increase in age (18-39 years – 68/1332; 5.1%; 40-59 years – 27/277; 9.7% and  $\geq 60$  years – 3/27; 11.1%; Figure 3). A similar trend in the increase in the number of individuals with antibody levels < 100 AU/mL was also noted (18-39 years – 383/1332; 28.8%; 40-59 years – 85/277; 30.7% and  $\geq 60$  years – 9/18; 33.3%) and the difference was not statistically significant (P=0.72; Figure 4).

A significantly higher proportion of individuals with diabetes mellitus and hypertension had negative antibodies as compared to those without (6/38; 16.0% with Diabetes vs 92/1598; 6.0% without diabetes; P=0.01 and 6/47; 13.0%; Figure 5 with hypertension and 92/1589; 6.0% without hypertension; P = 0.04; Figure 6). There was no significant difference in the number of individuals with Diabetes (14/463; 3.02% Vs. 24/1135; 2.11%; P=0.3) and Hypertension (13/464; 2.80% Vs. 34/1125; 3.02%; P=0.82) in the <100 AU/mL group as compared to the above 100 AU/mL group.

## Discussion:

This study was taken up to evaluate the levels of IgG anti-S1 and IgG anti-S2 antibodies to SARS-CoV-2 in healthcare workers who were fully vaccinated to assess the duration of vaccine induced immunity and protection against COVID-19. Analysis of antibody titres was done in individuals who were vaccinated with either Covishield or Covaxin. S1/S2 spike neutralizing antibodies were evaluated in the study group and categorized in to two: those with no antibodies (negative i.e., below the detection limit) and those with <100 AU/mL. This was based on our earlier experience where majority of the patients with <100 AU/mL were admitted with mild or moderate breakthrough infections.

A total 6.6% individuals were negative for antibodies after 6 months of 2nd dose vaccination. Studies from Israel<sup>3</sup>, the USA<sup>4</sup> and UK<sup>5</sup> also demonstrated decline in humoral response to BNT162b2 (Pfizer-BioNTech) and the Oxford AstraZeneca (ChAdOx1-S) and suggested a booster dose at 6 months after the 2nd dose of vaccination. In our study, approximately 30% individuals had less than 100 AU/mL indicating their risk of SARS-CoV-2 infection upon exposure, hence administering booster doses after 6 months may be beneficial in this group of individuals reducing the disease burden.

S1/S2 spike neutralizing antibody decline was noted across all age groups. However, a greater number of individuals above 40 years with comorbidities (diabetes and hypertension) were found to have significantly lower (less than 100AU/mL) or no antibodies, pointing to their risk of contracting the infection. Therefore, individuals above 40 years with diabetes and hypertension of both genders may be at a higher risk of SARS-CoV-2 infection and these individuals may be prioritized for a booster dose after 6 months.

Our results demonstrate decline in neutralizing antibodies in 30% of the individuals and 6.6% with no antibodies assessed at 6 months. A study from Israel reported decline in neutralizing antibody titres up to 42-46% in persons of 65 years of age or older and in persons <45 years age respectively. Based on their observation they administered a booster dose and demonstrated protection against COVID-19.<sup>6,7</sup> Our results suggest that enumerating antibody titres at 6 months especially in those with comorbidities would help in prioritizing such individuals for booster dosing

In conclusion, we demonstrate decline in antibody titres in 30% of individuals above 40 years of age after 6 months of vaccination. Therefore, these individuals need to be administered a booster dose at 6 months.

## Declarations

### Competing Interests

The authors declare no competing interests

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## Figures

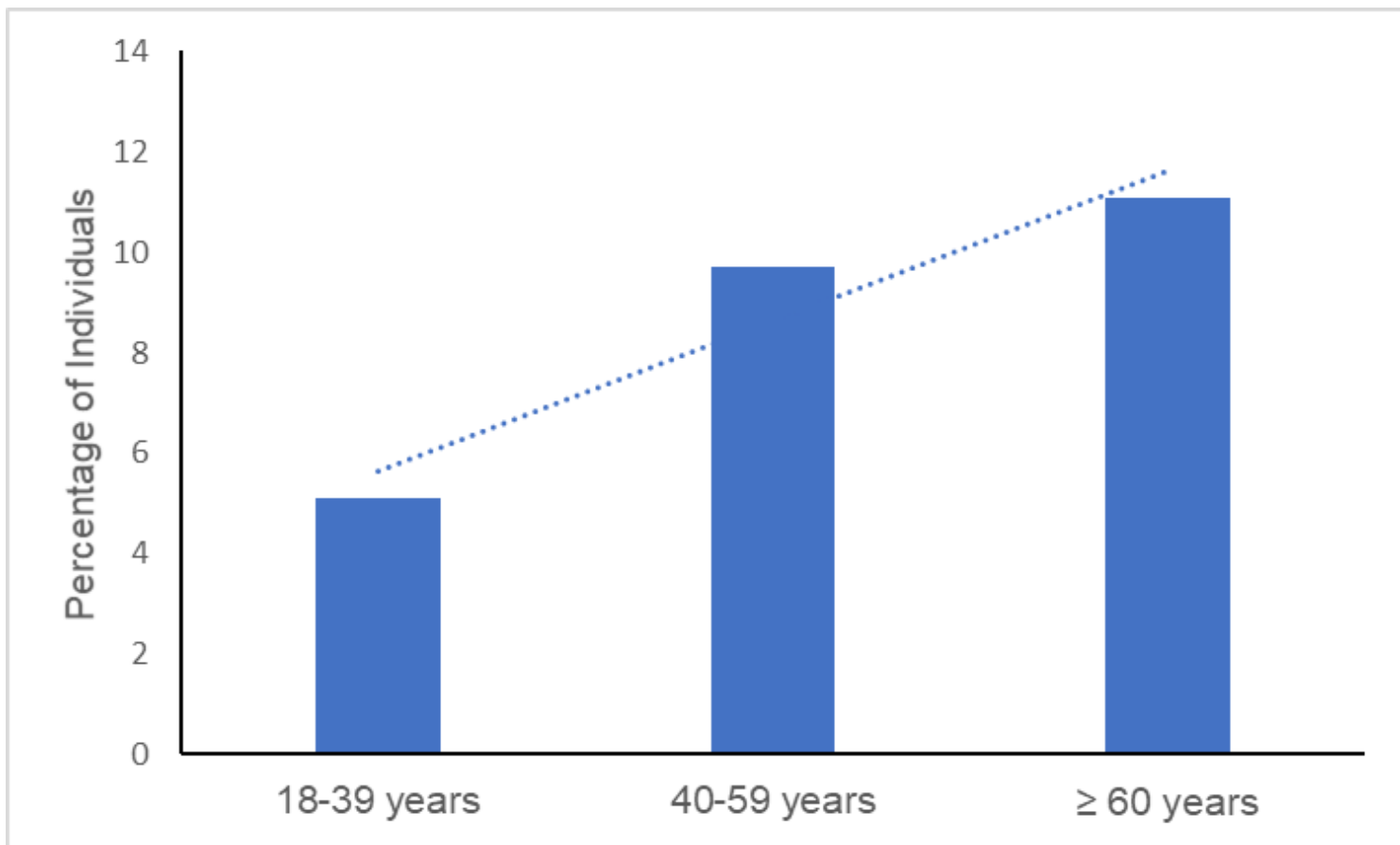
### Figure 1

**Percentage of individuals with negative antibody levels at six months post vaccination**

### Figure 2

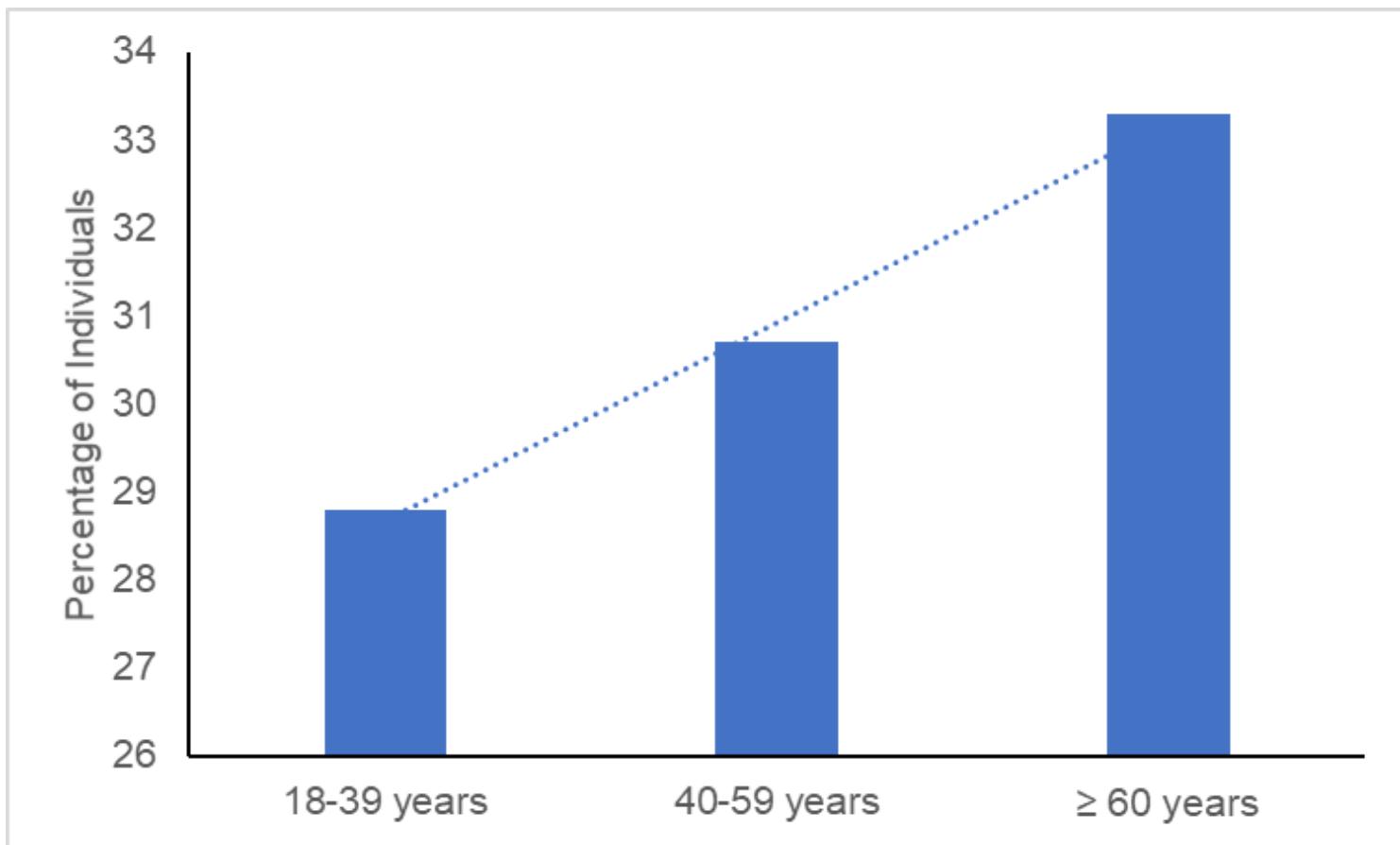
**Percentage of individuals with antibody levels <100 AU/mL at 6 months**

Comparison of individuals with negative S1/S2 spike neutralizing antibodies (below the detectable range) based on age revealed a significant ( $P=0.007$ ) increase in the number with increase in age (18-39 years – 68/1332; 5.1%; 40-59 years – 27/277; 9.7% and  $\geq 60$  years – 3/27; 11.1%; Figure 3). A similar trend in the increase in the number of individuals with antibody levels < 100 AU/mL was also noted (18-39 years – 383/1332; 28.8%; 40-59 years – 85/277; 30.7% and  $\geq 60$  years – 9/18; 33.3%) and the difference was not statistically significant ( $P=0.72$ ; Figure 4).



**Figure 3**

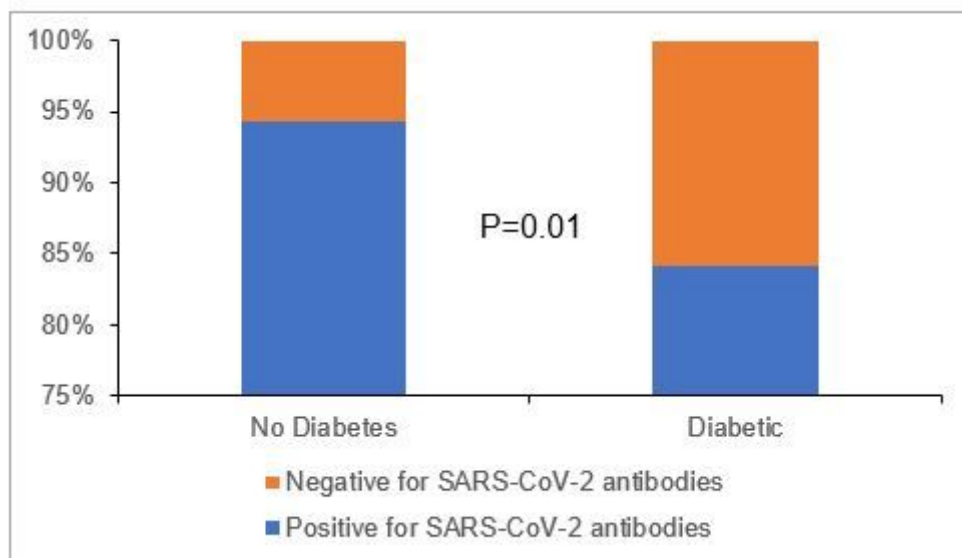
Percentage of individuals with negative antibody levels in different age groups



**Figure 4**

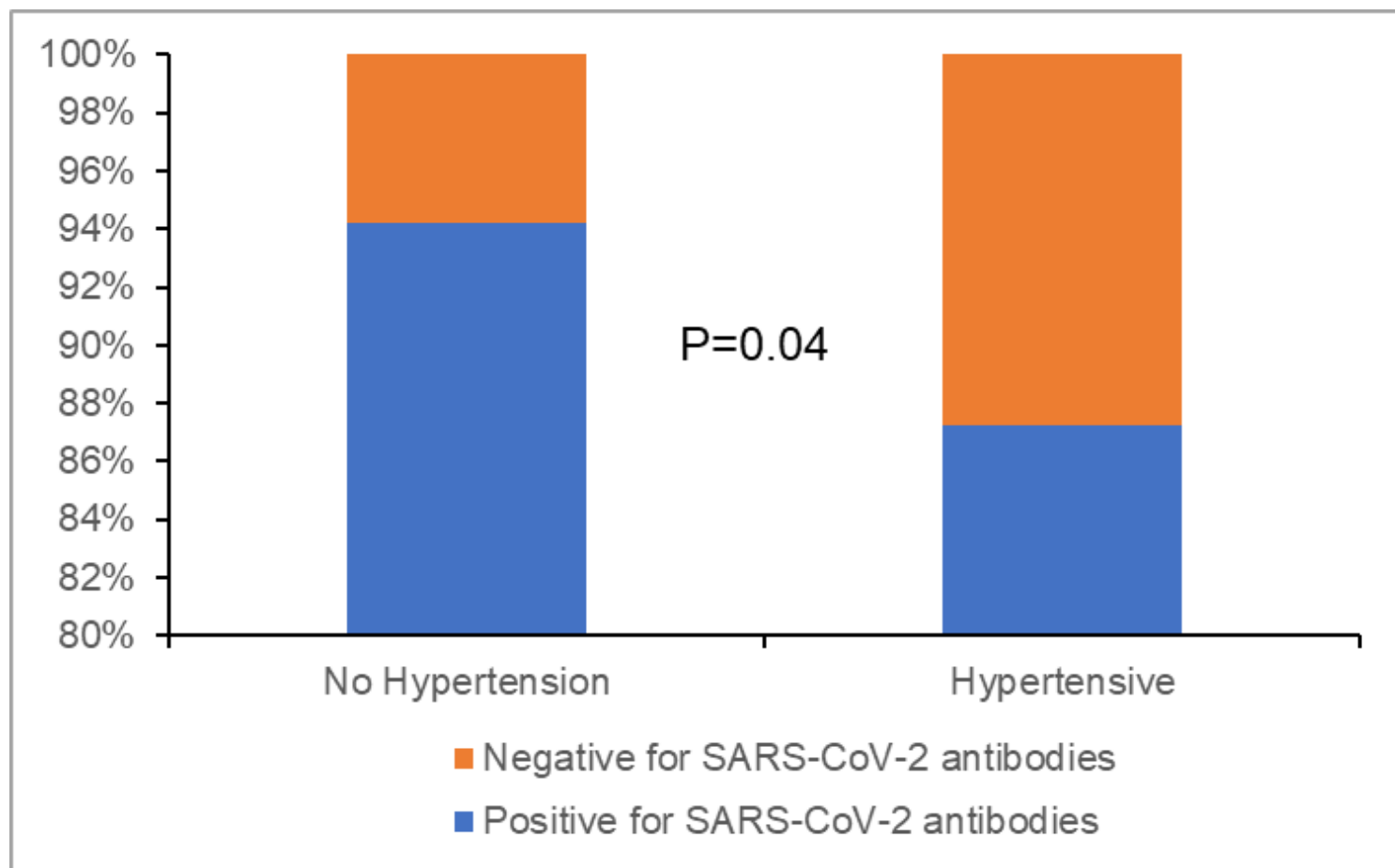
**Percentage of individuals with antibody levels <100 AU/mL in different age groups**

A significantly higher proportion of individuals with diabetes mellitus and hypertension had negative antibodies as compared to those without (6/38; 16.0% with Diabetes vs 92/1598; 6.0% without diabetes;  $P=0.01$  and 6/47; 13.0%; Figure 5 with hypertension and 92/1589; 6.0% without hypertension;  $P = 0.04$ ; Figure 6). There was no significant difference in the number of individuals with Diabetes (14/463; 3.02% Vs. 24/1135; 2.11;  $P=0.3$ ) and Hypertension (13/464; 2.80% Vs. 34/1125; 3.02%;  $P=0.82$ ) in the <100 AU/mL group as compared to the above 100 AU/mL group.



**Figure 5**

Percentage of individuals with negative antibody levels with and without Diabetes



**Figure 6**



Percentage of individuals with negative antibody levels with and without Hypertension