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Short communication

Duration of anti-SARS-CoV-2 antibodies much shorter in India

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Abstract

Seroprevalence survey, for antibodies to SARS-CoV-2, of healthcare workers (HCW) working in three Government run hospitals in Mumbai was carried out in June 2020. Among the 801 HCWs tested, seroprevalence was 11.1%. Males (13.5% vs. 8.9% in females) and ancillary workers (18.5% vs 6.9% in doctors and nurses) were more likely to be seropositive. Sixty-two (7.74%) had been previously diagnosed with RT PCR test for SARS-CoV-2. Of these, 44 (71%) were seronegative. Upto 28 days after a positive PCR test, 90% of subjects were found to be seropositive. This reduced to less than half (38.5%) between 29 and 42 days. None of 28 infected HCWs who had the RT-PCR more than 50 days ago tested positive for antibodies. It seems likely that cellular immunity plays a larger role in defence against the illness.

Humoral immune response to SARS-CoV-2 infection have been reported to be variable, but short-lived [1–4]. We carried out a seroprevalence survey of healthcare workers (HCW) working in three Government run hospitals in Mumbai. Pan immunoglobulin Elecsys Anti-SARS-CoV-2 Assay (Roche Diagnostics, Rotkreuz, Switzerland) using recombinant protein representing the nucleocapsid (N) antigen in double antigen sandwich assay format was done after informed consent. This test has a specificity of 99.8% and 100% sensitivity for patients, fourteen days post-PCR confirmation. The result is given as a cut off index (Col), and is then interpreted either as reactive/positive (Col > 1.0) or non-reactive/negative (Col < 1.0) [5]. We did not test for the antibodies against S antigen. A pretested, validated questionnaire in local language was used to collect data on demographic details and symptoms.

The study was approved by Institutional Ethics Committee of the JJ group and Grant Medical College, Mumbai, India.

Among the 801 HCWs who got tested, seroprevalence was 11.1%. Males (13.5% vs. 8.9% in females) and ancillary workers (18.5% vs 6.9% in doctors and nurses) were more likely to be seropositive (Table 1).

There was significantly higher seroprevalence in those previously diagnosed with COVID-19 with a positive PCR test compared to those who had not been tested by RT-PCR; 29% (CI 19.2–41.4) compared to 9.6% (CI 7.7–12.1). Sixty-two (7.74%) had been previously diagnosed with RT PCR test for SARS-CoV-2. Of these, 44 (71%) were seronegative. Individuals who were symptomatic in the last 30 days with any of the symptoms associated with COVID-19 had a significantly higher seropositive rate; 16.8% (CI 11.8–23.2) compared to 9.6% (CI 7.6–12.2). Sub-analysis of the various symptoms indicates that only loss of smell or taste and presence of non-specific febrile illness in the last 30 days were significant variables associated with higher seroprevalence. None of the other symptoms associated with COVID-19 were statistically significant (Table 2).

Subjects who had visited a fever clinic in the last 30 days had a significantly higher seroprevalence; 20.5% (CI 14.4–28.2) compared to 9.3% (CI 7.3–11.7). Individuals with a family member living in the same house diagnosed with COVID-19 had a significantly higher seroprevalence; 18.9% (CI 11.5–29.4) compared to 10.3% (CI 8.3–12.8). Having a COVID-19 patient living within 50 m of the individual’s residence was not a significant factor for increased seroprevalence (see Table 3).

Duration between positive RT-PCR test and serological testing ranged from 15 to 49 days for 34 (54.8%), and >50 days in 28 subjects. Upto 28 days after a positive PCR test, 90% of subjects were found to be seropositive. This reduced to less than half over next two weeks (38.5%) between 29 and 42 days. This further reduced to less than 15% for subjects who were tested between 43 and 49 days of their positive RT-PCR. None of the 28 infected HCWs who had had the RT-PCR test more than 50 days ago tested positive for the antibodies. Of the people who had never been RT PCR positive, 9.6% had antibodies (Table 4). The mean antibody levels of people who had never been tested for RT PCR were 26.77 Col (28.47 Col in those with RT PCR test positive).

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Our findings are in agreement with the view that humoral response is launched rapidly and peaks at about 3–4 weeks with an exponential decline thereafter [1–4]. This however is in contrast to the findings of Gudbjartsson et al. in Iceland where more than 90% of persons with previously positive RT PCR tests had neutralizing antibodies after 4 months [4]. Nearly 9.6% of HCWs have been asymptomatic and never tested with RT PCR but had anti SARS-CoV-2 antibodies indicating asymptomatic infections. Antibody levels in such asymptomatics are similar to levels seen in symptomatics which is contrary to findings by Long et al. [2].

### Table 1
Seroprevalence as per different demographic and comorbidity characteristics.

| Group                  | All | Sero (–) | Sero (+) | % (+) | 95% CI   | p value | Odds ratio |
|------------------------|-----|----------|----------|-------|----------|---------|------------|
| All                    | 801 | 712      | 89       | 11.1  | 9.1–13.5 |         |            |
| Occupation             |     |          |          |       |          |         |            |
| Ancillary workers      | 292 | 238      | 54       | 18.5  | 14.5–23.3| Odds = 0.227 |
| Doctors                | 201 | 187      | 14       | 7.0   | 4.2–11.4 | OR = 2.65  |
| Nurses                 | 308 | 287      | 21       | 6.8   | 4.5–10.2 | OR = 2.71  |
| Gender                 |     |          |          |       |          |         |            |
| Male                   | 386 | 334      | 52       | 13.5  | 10.4–17.3| p = 0.04  OR = 1.51 |
| Female                 | 415 | 378      | 37       | 8.9   | 6.5–12.1 |          |            |
| Age group              |     |          |          |       |          |         |            |
| 20–40 years            | 413 | 372      | 41       | 9.9   | 7.4–13.2 | p = 0.54  OR = 0.803 |
| 40–60 years            | 380 | 333      | 47       | 12.4  | 9.4–16.1 |            |            |
| >=60 years             | 8   | 7        | 1        | 12.5  | 2.2–47.1 |            |            |
| Comorbidities          |     |          |          |       |          |         |            |
| None                   | 682 | 604      | 78       | 11.4  | 9.3–14.1 | 0.49     |            |
| Single                 | 103 | 94       | 9        | 8.7   | 4.5–16.0 | 0.62     |            |
| Multiple               | 16  | 14       | 2        | 12.5  | 2.2–37.3 |          |            |
| Cancer                 | 5   | 4        | 1        | 20.0  | 2.0–64.0 | 0.94     |            |
| Immunosuppression      | 11  | 9        | 2        | 18.2  | 4.0–48.9 | 0.45     |            |
| Asthma                 | 35  | 32       | 3        | 8.6   | 2.2–23.1 | 0.67     |            |
| Cardiac problems       | 48  | 44       | 4        | 8.3   | 2.8–20.1 | 0.56     |            |
| Diabetes mellitus      | 38  | 35       | 3        | 7.9   | 2.0–21.5 | 0.56     |            |

### Table 2
Seroprevalence and associated factors.

| Group                  | All | Sero (–) | Sero (+) | +ve (%) | 95% CI   | p value | Odds ratio |
|------------------------|-----|----------|----------|---------|----------|---------|------------|
| PCR positive individuals |     |          |          |         |          |         |            |
| COVID PCR (+)          | 62  | 44       | 18       | 29.0   | 19.2–41.4| 0.000003 |
| COVID PCR (–)          | 739 | 668      | 71       | 9.6    | 7.7–12.0 | OR = 3.02 |
| Symptomatic in last month | 167 | 139      | 28       | 16.8   | 11.8–23.2| 0.0001  |
| Asymptomatic in last month | 634 | 573      | 61       | 9.6    | 7.6–12.2 | OR = 2.655|
| Symptoms associated with seropositivity |     |          |          |         |          |         |            |
| Loss of taste/smell    | 10  | 4        | 6        | 60.0   | 31.2–83.3| 0.0003  |
| No loss of taste/smell | 791 | 708      | 83       | 10.5   | 8.5–12.8 | OR = 2.71 |
| Acute Febrile Illness  | 28  | 15       | 13       | 46.4   | 29.5–64.2| 0.000002 |
| No acute Febrile Illness | 773 | 697      | 76       | 9.8    | 7.9–12.1 | OR = 1.51 |
| Any Acute Respiratory Illness | 97  | 83       | 14       | 14.4   | 8.7–22.9 | 0.26     |
| No acute Respiratory Illness | 704 | 629      | 75       | 10.7   | 8.6–13.2 |          |            |
| Acute Respiratory Illness – SARI | 16  | 13       | 3        | 18.8   | 5.8–43.8 | 0.59     |
| Acute Respiratory Illness – ILI | 81  | 70       | 11       | 13.6   | 7.6–22.9 |          |            |
| Non-specific illness   | 90  | 78       | 12       | 13.3   | 7.6–22.0 | 0.47     |
| No Non-specific illness | 711 | 634      | 77       | 10.8   | 8.7–13.3 |          |            |
| Acute Gastric/enteric illness | 8   | 7        | 1        | 12.5   | 0.1–49.2 | 0.83     |
| No acute gastric/enteric illness | 793 | 705      | 88       | 11.1   | 9.1–13.5 |          |            |
| Eye Redness            | 12  | 11       | 1        | 8.3    | 0.0–37.5 | 0.84     |
| No Eye Redness         | 789 | 701      | 88       | 11.2   | 9.1–13.6 |          |            |
| Skin rash              | 9   | 8        | 1        | 11.1   | 0.0–45.7 | 0.91     |
| No skin rash           | 792 | 88       | 704      | 88.9   | 86.5–90.9|          |            |

### Table 3
Seroprevalence based on exposure.

| Group                  | All | Sero (–) | Sero (+) | (+) % | 95% CI   | p value | Odds ratio |
|------------------------|-----|----------|----------|-------|----------|---------|------------|
| Risk/exposure characteristics |     |          |          |       |          |         |            |
| Visited Fever clinic    | 132 | 105      | 27       | 20.5  | 14.4–28.2| 0.0002  OR = 2.52 |
| Not visited fever clinic | 669 | 607      | 62       | 9.3   | 7.3–11.7 |          |            |
| Household person positive | 74  | 60       | 14       | 18.9  | 11.5–29.4| 0.02 OR = 2.03 |
| No household person positive | 727 | 652      | 75       | 10.3  | 8.3–12.8 |          |            |
| Neighbourhood person positive | 397 | 348      | 49       | 12.3  | 9.4–16.0 | 0.27     |
| No Neighbourhood person positive | 404 | 364      | 40       | 9.9   | 7.3–13.2 |          |            |
bility of subjects to re-infection after antibody response has subsided is a matter of investigation, but has shown to be unlikely in rhesus experimental models [6]. Since the reported rates of re-infection are quite low, it is possible that cellular immunity or antibodies to the S antigen may play a greater role in defence against COVID 19.

Key findings

(1) Humoral antibody response to SARS-CoV-2 is much shorter in Indian population as compared to previously reported.
(2) Cellular immunity or other antibodies may play a larger role in providing protection against the disease.
(3) These facts need to be kept in mind before planning vaccine studies.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Table 4
Weekwise anti SARS-CoV-2 antibody levels in Healthcare workers in Mumbai, India.

| Days after (+)ve RT-PCR Test | No. Of persons | Positives* | Antibody levels mean (std dev) COI | Outliers’ n (values) |
|-----------------------------|----------------|------------|-----------------------------------|----------------------|
| 15–21                       | 5              | 3          | 1.01 (1.61)                       | 1 (14.26)            |
| 22–28                       | 11             | 9          | 31.7 (31.3)                       | 1 (0.08)             |
| 29–35                       | 7              | 2          | 0.93 (1.81)                       | 1 (73)               |
| 36–42                       | 6              | 1          | 0.1 (0.1)                         | 1 (12.91)            |
| 43–49                       | 6              | 1          | 0.1 (0.03)                        | 1 (28.93)            |
| 50–56                       | 9              | 0          | 0.07 (0.01)                       | 0                    |
| >56                         | 18             | 0          | 0.08 (0.01)                       | 2 (0.92, 0.12)       |

* COI > 1 is considered positive.

Outliers have not been included in the calculation of mean and std. dev.