4th National Sero Survey of India: Vaccine Generated Antibodies Enhancement

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ABSTRACT

The results of the fourth COVID-19 national serosurvey (June-July 2021) of India have been analysed. Much needed data of vaccine generated antibodies have been reported world first as recorded in Indian population on the ground in real. More than two-thirds of (67.6%) Indian population developed antibodies against the infection. This includes natural immunity build up due to infection and vaccine generated antibodies. Eleven states: Madhya Pradesh, Rajasthan, Bihar, Gujrat, Chhattisgarh, Uttarakhand, Uttar Pradesh, Andhra Pradesh, Karnataka, Tamil Nadu, and Odisha had sero positivity of >67.6% which was the national average. Ten other states registered < 67.6% seroprevalence were: Punjab, Telangana, Jammu and Kashmir, Himachal Pradesh, Jharkhand, West Bengal, Haryana, Maharashtra, Assam, and Kerala. Single dose vaccination of 24% population added 19% seroprevalence in the population whereas 13% full vaccination increased 28% individuals registered antibodies. The highest (90%) seroprevalence was registered among the individuals who have taken both vaccine doses followed by HCWs (85%). Seroprevalence in 85-90% population might be the threshold for herd immunity which delayed or possibly stopped the third COVID-19 wave in India.

Keywords: COVID-19 seroprevalence, fourth serosurvey, herd immunity, SARS-CoV-2 spread, serosurvey of India.

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I. INTRODUCTION

In the fifth wave of infection, on July 29, 2021, Japan reported [1] more than 10,000 new novel coronavirus cases, which is the highest tally registered so far in all the previous four waves of the pandemic. The share of the capital city Tokyo with more than 3,000 new cases was also a record high. The more contagious Delta variant which spread faster was the reason for the surge in the new cases. The area surrounding Tokyo also saw a higher number of cases. Kanagawa, Saitama, and Chiba registered 1,164, 864, and

506 cases, respectively. Prefectures Osaka and Okinawa also logged a record number of 932 and 392 cases, respectively. The Delta variant is responsible for 70% of the cases in the above areas of Japan. In the city of London (UK), in July 2021, the delta variant drove [2] the cases higher though hospitalization and deaths remained low due to a high vaccination rate. The daily new cases (7-day average) were about 5,000. A similar situation was noticed in another large city, New York (US), where cases started increasing in July. The higher transmissibility of the Delta variant was also the reason for the surge in New York [3], [4]. Novel coronavirus

cases surged [5] in Israel in July even though 60% [6] of the population was fully vaccinated. The rise in the cases was attributed to the emergence of the Delta variant. Israel has begun administering booster shots to people above 60 years. The Delta variant also caused a surge across the US [7]. Elsewhere in Bangladesh, the COVID-19 cases surged [8] to a new high in June-July. On July 25, 2021, in a new wave, Bangladesh reported 228 deaths and 11,291 new cases. A countrywide shutdown was imposed for 14 days to contain the virus. The city of Dhaka counted 69 deaths followed by the city of Khulna with 50 fatalities. The cumulative caseload stood at 1,164,635. As of August 4, Indonesia surpassed [9], [10] 100,000 COVID-19 deaths and caseload above 3.5 million. Challenging situation arose due to highly contagious Delta variant. In Indonesia, the deaths doubled in just over nine weeks, whereas earlier, the pandemic death toll of 50,000 registered at the end of May was reached in 14 months.

In India, ten states: Kerala, Maharashtra, Karnataka, Tamil Nadu, Odisha, Assam, Mizoram, Meghalaya, Andhra Pradesh, and Manipur reported [11] an increase in daily infections whereas in other states the cases were either remained the same or decreased in the receding second wave. The states were preparing for a possible third wave and simultaneously ramping up the vaccination drive. When the second wave receded after the cases dropped below 40,000 [12] for a few days, the daily new cases started rising again. On July 29, 44,681 cases were registered, up again from a low of 37,680 recorded on July 25. This indicated a growing pattern of infections and a fear of a third wave. India recorded a 7.5% weekly rise in cases in twelve weeks [13] after the second wave receded. There is a fear of a spike in the cases leading to a third wave of the pandemic. While the second wave is receding [14] in all of India, the situation in Kerala is alarming. On July 28, Kerala contributed 51% new caseload to India's total. The positivity rate of Kerala is above 10 and R_0 (rate of the spread) is above one. The seropositivity in Kerala is the lowest at 44.4%, compared to the country's average of 67.6%. Lower seroprevalence in Kerala is indicative that Kerala has the most untapped population for the virus spread. The COVID-19 in Kerala can be prevented only by a speedy vaccination drive. Because of developed health infrastructure of Kerala compared to all of India, the case fatalities rate (CFR) is lowest at 0.4 and 0.49% in the first and second wave, respectively. Since the novel coronavirus was first reported in the Chinese city of Wuhan, the cumulative global novel coronavirus cases reached >195 million with worldwide the death tally hitting >0.41 million as of July 26 [15].

In a recently conducted [16] research of analyzing the data from an Italian town (Vo'; Padua) it was found that in both symptomatic and asymptomatic COVID-19 infections the antibodies' level remained high in detectable amount for nine months. 98.8% of people infected had antibodies in a detectable amount. Symptomatic infection activating the immune system to produce more antibodies was not established as suggested before. However, the titers of antibodies declined in 3-4 months. Reinfection could boost the antibodies level. Only one in four infected people passed the virus to a family member and 80% of transmission occurred through just 20% of infections. The study suggested that social distancing, use of masks, and limiting the contacts

minimized the spread. The vaccination effects became apparent [17] in Japan as the share of the people in the age group 65 and plus to new coronavirus caseload dropped sharply from 22 to 3.7% after 75% population of the above age group was vaccinated with at least one dose. The drive was launched in April, 2021 to vaccinate the elderly population with mRNA vaccines (Pfizer and Moderna). Germany started [18] in September, 2021 giving COVID-19 vaccine (Pfizer or Moderna) booster shots to the vulnerable population. Mixing of the vaccines has also been allowed [19] in Germany on efficacy grounds. Citizens who have received jabs of other makers were strongly suggested to take mRNA (Pfizer or Moderna) vaccines. In Germany, 52% of the citizens have been fully vaccinated and 62% have received one dose. Children between the age 12-17 will be inoculated voluntarily. In this age group, already 10% of children have been fully vaccinated. Canada and the US are the other countries that have started vaccinating children above 12. Because of the robust vaccination strategy in Germany, the delta variant did not cause much damage as happened in other parts of the globe.

Japan government has planned [20], [21] to inoculate Moderna vaccine to children in the age group 12-17. Japan has already allowed the Pfizer vaccine for emergency use for children aged 12 and above since June 1, 2021. Moderna's clinical trial showed that the vaccine was 100% effective and safe. In a clinical trial involving more than 2,200 adolescents, Pfizer's vaccine was also found to be 100% effective. The two mRNA vaccines (Pfizer and Moderna) are being developed for babies and younger children under age 12. Apart from vaccine development, much progress has been made in the treatment aspect of the disease. Japan has authorized monoclonal antibodies developed by Regeneron Pharmaceuticals Inc. (US). Chugai Pharmaceutical Co. (Japan) is in charge of the domestic sales of the drug in Japan. The neutralizing antibodies cocktail mixture is the combination of casirivimab and imdevimab given intravenously which acts against novel coronavirus's spike proteins. The injection drug is useful for mild to moderate conditions. The other three drugs approved in Japan to treat COVID-19 patients are remdesivir, dexamethasone, and baricitinib. Celltrion Inc. (South Korea) has been granted [22], [23] priority to its monoclonal antibody regdanvimab (CT-P59) for COVID-19 treatment by Health Canada. In phase 3 trial regdanvimab lowered the COVID-19 hospitalization risk by 72% in patients with a disease progression. The drug also decreased the clinical recovery time of COVID-19 patients. The company Celltrion Inc. is also developing neutralizing antibody cocktail with regdanvimab for novel coronavirus variants that emerged recently.

Large sample size with 450,000 individuals participating in COVID-19 serosurvey was conducted [24] of self-referred individuals in 3 mega cities (Delhi, Mumbai, Kolkata) and 9 big cities (Ahmedabad, Jaipur, Bangalore, Chennai, Pune, Coimbatore, Surat, Visakhapatnam, Nagpur) of India in June-December 2020. In articles [25], [26], the analysis of the above results has been described. The seroprevalence was as high as 63.8% in Bangalore followed by Delhi (54.9%), and Kolkata (54.6%). In Kolkata, Mumbai, Chennai, Pune, Coimbatore, Surat, Visakhapatnam, and Nagpur, the

seroprevalence reached a plateau value after 4 months. It decreased as antibodies waned out in some residents while in Bangalore, Jaipur, Ahmedabad, and Delhi seropositivity showed a monotonous increase. In article [27], the serosurvey of Mumbai slums (Dharavi and Cuffe Parade) was presented. The seropositivity in the slums was 75% which made the slums near the COVID-19-free zone justified the concept of herd or mass immunity on the ground. The high infection rate in Kerala compared to the other Indian states has been validated by the newly established “Health Index Theory” [28], [29]. The COVID-19 virus stability under different conditions and sanitization methods [30] and the possibilities [31] of the virus transmission from humans to pets and vice versa have also been described. Initial COVID-19 vaccine preparation attempts [32], vaccine development [33] and the application of supercomputer in containing the pandemic [34] have also been studied.

In this research article, we have discussed the data and the results of the fourth national serosurvey of India conducted between June-July 2021. The data presented can be used for the COVID-19 response at the state and national levels. From the data, we can know the extent of the spread of the disease.

II. METHODS

The fourth national serosurvey was conducted by Indian Council of Medical Research (ICMR) in the period June-July 2021. The survey covered 28,975 citizens (general population) and 7,252 healthcare workers. A total of 8,691 children were surveyed. It was conducted all across India in 21 states covering 70 districts. The districts and states were the same as covered in last three national surveys. The bars and plots shown in this article were constructed from the above sero survey results.

III. RESULTS AND DISCUSSION

A. State-wise Seroprevalence

Fig. 1 shows that more than two-thirds (66.6%) population of 11 states of India have developed [35] SARS-CoV-2 antibodies. Both natural infection by virus and vaccination might have contributed to the antibodies generation. As of mid-July, 13% adult population was fully vaccinated whereas 24% took one dose [36]. Madhya Pradesh has the highest seroprevalence of 79% while Kerala has the lowest of 44.4%. In Assam and Maharashtra seroprevalence were 50.3 and 58%, respectively [37]. The seroprevalence in other states were as follows: Rajasthan (76.2%), Bihar (75.9%), Gujarat (75.3%), Chhattisgarh (74.6%), Uttarakhand (73.1%), Uttar Pradesh (71%), Andhra Pradesh (70.2%), Karnataka (69.8%), Tamil Nadu (69.2%), and Odisha (68.1%). The states with < 66.6% seroprevalence were Punjab, Telangana, Jammu and Kashmir, Himachal Pradesh, Jharkhand, West Bengal, Haryana, Maharashtra, Assam, and Kerala. The values of seroprevalence of different states have been given in Fig. 1.

Fig. 1. State-wise seroprevalence recorded in fourth national serosurvey.

B. Age-wise Seroprevalence

It was found that children in the age groups 6-9 and 10-17 years had seroprevalence of 57.2% and 61.6%, respectively (Fig. 2). The age-wise distribution of seroprevalence for adult population was 66.7% for 18-44, 77.6% for 45-60, and 76.7% for >60 years.

C. Gender-, Rural- and Urban-wise Seroprevalence

Gender, rural, and urban disaggregated seroprevalence have been given in Fig. 3. The seroprevalence in females was more (69.2%) than in males (65.8%). Gender-wise the pattern is similar to that found in 3 mega and 9 big cities of India in the survey conducted between July-December 2020 [25], [26]. The seroprevalence in females was 34.6% and 29.9% in males. The antibodies in women were more than in men in the slum and non-slum population of Mumbai [27]. The higher sero prevalence in urban (69.6%) than in rural (66.7%) areas was due to crowded places and closed spaces where close contacts were more in urban localities than in villages.

Fig. 2. Age-wise distribution of seroprevalence found in fourth national serosurvey.

Fig. 3. Gender-wise and rural and urban seroprevalence registered in fourth national serosurvey.

D. Data Analysis of the Fourth Survey (Contribution of Vaccination)

Fig. 4 shows the sero survey results of unvaccinated, one dose (partially), and two doses (fully) vaccinated population. The data have not been normalized to the adult vaccination and the sero survey which included the age group 6-17 years. One dose and two doses seroprevalence were of adult population. Among unvaccinated population, 62% had antibodies. Inoculating one vaccine shot, 81% people developed antibodies whereas antibodies prevalence rose to 90% in fully (two-dose) vaccinated population. The increasing order of seroprevalence was: unvaccinated (62%) < one dose vaccinated (81%) < two doses vaccinated (90%). One dose vaccination enhanced the antibodies in 19% population while two doses generated antibodies in 28% of individuals. Two-dose vaccination enhancement was more than a single dose. Upon inoculating a second dose the antibodies' production was more which is very natural since if one dose vaccination or natural virus infection could not generate enough antibodies to the detection level then a second dose acts as a booster. Fig. 5 compares the registered antibodies enhancement by one and two doses and the vaccination record. 24% single dose vaccination generated antibodies in 19% population whereas 28% enhancement was achieved when 13% of the population was covered by the second shot.

Fig. 4. Seroprevalence in unvaccinated, 1 dose and 2 dose vaccinated population.

Fig. 5. Comparison of 1 dose and 2 doses seroprevalence increase as recorded by observation and vaccine inoculation record.

E. Antibodies in Healthcare Workers (HCWs)

The seroprevalence in HCWs and the general population has been compared in Fig. 6. One dose and two-dose data were the same as explained in Fig. 4. The seroprevalence in HCWs was lower at 85% than the fully vaccinated general population which had a 90% prevalence. The reason for lower seroprevalence in HCWs was because 10% HCWs were not vaccinated. The seroprevalence in all over India can go up to 97% as recorded in a recently concluded survey of Delhi's population [38]. The recorded high seroprevalence of 80-97% generated by virus infection and vaccination (one and two-dose) combined has delayed and possibly stopped the third wave of the pandemic in India. 80-97% sero prevalence is well above the herd immunity threshold that can stop the spread of the highly transmissible Delta variant. The seroprevalence in the range 80-97% was good enough to make up the antibodies' decay over the time and vaccine breakthrough infections.

Fig. 6. Comparison of seroprevalence in healthcare workers (10% unvaccinated) and 1 dose and 2 doses vaccine inoculation seroprevalence.

F. Comparison of First, Second, Third, and Fourth National Serosurveys Conducted by ICMR

The results of all the four national surveys have been given in Fig. 7. The first sero survey, conducted between May-June 2020, reported that 0.73% of the adult population had SARS-CoV-2 antibodies. The second survey done between August-

September 2020 increased seroprevalence to 7.1%. The seroprevalence further increased to 24.1% as registered in the third survey carried out between December 17, 2020-January 8, 2021. The third serosurvey showed the generation of antibodies only by infection as vaccination in India started in the middle of January 2021 [39]. The results of the fourth survey conducted in the period June-July 2021 revealed that nearly two-thirds (67.6%) population had SARS-CoV-2 antibodies developed either by infection or vaccination or infection and vaccination combined. The first national sero survey was conducted in adults, in the third survey children above 10 were included, and in the fourth survey children in the age group 6 and above were registered. The fourth sero prevalence data had contribution from virus infection and vaccination both as vaccination drive already inoculated 13% population with two-dose and 24% had one dose regime when the survey was undertaken. Apart from infections and vaccines, the antibodies found in the population had a share from vaccine breakthrough (in fourth survey) and reinfections (in all the four surveys) though a very small percentage. Fig. 8 is the plot of sero-positivity versus the time in months constructed from Fig. 7. The rate of developing antibodies in the population was slower in the beginning and more people developed antibodies with time. The spread of the virus was faster in the later stage due to the high active caseload in the population.

Fig. 7. Seroprevalence versus time from May 2020- July 2021.

STATEMENTS

The data and results in this article are very reproducible. Author (Zameer Shervani, Ph.D.) is Director of Food & Energy Security Research & Product Center, Sendai, Japan. Authors have qualifications; Deepali Bhardwaj MBBS, MD, DVDL, M.Phil.; Abdullah Sherwani B.Tech.; Intazam Khan MBBS; Umair Yaqub Qazi Ph.D.; Sadia Hasan, Ph.D.; Roma Nikhat MCA; Ankira Agarwal MBBS; Aiman Ibrahim MBBS; Adil Ahmed Khan MBBS.

Fig. 8. Increase of seroprevalence with time (month) recorded in different serosurveys.

REFERENCES

- [1] Japan logs over 10,000 new COVID cases as Tokyo hits record 3,865. [Internet] [cited July 29, 2021] The Japan Times.
- [2] London's delta surge should jolt New York. [Internet] [cited July 26, 2021] The Japan Times.
- [3] <https://data.london.gov.uk/dataset/coronavirus-covid-19-cases>.
- [4] Tracking Coronavirus in New York: Latest Map and Case Count. [Internet] [cited August 2, 2021] The New York Times.
- [5] Israel issues travel warning for U.S. over COVID-19 concerns. [Internet] [cited August 4, 2021] REUTERS.
- [6] Our World in Data COVID-19 Vaccinations.
- [7] Our World in Data COVID-19; Daily new confirmed cases per million people; United States.
- [8] Covid-19 continue to rise, hospitals may run out of capacity; Bangladesh govt. [Internet] [cited July 25, 2021] Hindustan Times.
- [9] Indonesia surpasses 100,000 deaths amid new virus wave. [Internet] [cited August 4, 2021] The Associated News.
- [10] Worldometer-coronavirus-Indonesia.
- [11] Centre asks states with high Covid caseloads to impose stricter curbs. [Internet] [cited August 1, 2021] Hindustan Times.
- [12] India's 7-day average of Covid cases crosses 40,000 again. [Internet] [cited July 31, 2021] The Times of India.
- [13] After 11 weeks of decline, Covid cases see 7.5% surge. [Internet] [cited August 2, 2021] The Times of India.
- [14] Why has Kerala been unable to contain Covid?, [Internet], [cited on July 31, 2021] The Times of India.
- [15] <https://www.worldometers.info/coronavirus/>.
- [16] Covid-19 antibodies last at least nine months after infection, here's how. [Internet] [cited July 20, 2021] Hindustan Times.
- [17] Covid-19 infections decrease sharply among vaccinated older people. [Internet] [cited July 22, 2021] The Japan Times.
- [18] 16 German states to offer booster dose against Covid-19 to 'vulnerable citizens. [Internet] [cited August 3, 2021] Hindustan Times.
- [19] Germany issues world's strongest recommendation for mixing Covid-19 vaccines. [Internet] [cited July 2, 2021] CNN Digital Online News.
- [20] Japan to lower minimum age for Moderna vaccine to 12. [Internet] [cited July 15, 2021] The Japan Times.
- [21] Japan health ministry panel backs lowering Moderna vaccine age limit to 12. [Internet] [cited July 19, 2021] The Japan Times.
- [22] South Korea's Celltrion gets approval for phase 3 trials of COVID-19 antibody drug. [Internet] [cited October 12, 2021] The Asahi Shimbun.
- [23] Celltrion obtains priority review in Canada for Covid-19 drug regdanvimab. [Internet] [cited August 3, 2021] Pharmaceutical Technology.
- [24] Velumani A, Nikam C, Suraweera W, Fu SH, Gelband H, Brown PE, et al. SARS-CoV-2 Seroprevalence in 12 Cities of India from July-December 2020. *medRxiv*. 2021.
- [25] Shervani Z, Bhardwaj B, Nikhat R. COVID-19 Infection in India: Seropositivity versus the Dynamics of the Spread. *European Journal of Medical and Health Sciences*. 2021; 3(4): 95-99.
- [26] Shervani Z, Bhardwaj D, Sherwani A, Khan I, Qazi UY. COVID-19 Infection in 8 Big Cities of India: The Dynamics of the Spread and Seropositivity. *European Journal of Medical and Health Sciences* 2021; 3(6): 1-5.
- [27] Shervani Z, Bhardwaj D, Nikhat R. Dharavi Slums (Mumbai, India): The Petri Dish of COVID-19 Herd Immunity. *European Journal of Medical and Health Sciences*. 2021; 3(3): 38-41.

- [28] Shervani Z. COVID-19 in Kerala: Health Index Theory. *European Journal of Medical and Health Sciences*. 2021; 3(2): 21-24.
- [29] Shervani Z. COVID-19 in Kerala: The Dynamics of Spread and Health Index Theory. *RAS Medical Science*. 2021; 1(2): 1-3.
- [30] Shervani Z, Khan I, Siddiqui NY, Khan T, Qazi UY. Viability of SARS-CoV-2 and Sanitization Methods. *European Journal of Medical and Health Sciences*. 2021; 3(1): 22-27.
- [31] Shervani Z, Khan I, Siddiqui NY, Khan T, Qazi UY. Risk of SARS-CoV-2 Transmission from Humans to Pets and Vice Versa. *European Journal of Medical and Health Sciences*. 2021; 3(1): 34-38.
- [32] Shervani Z, Khan I, Qazi UY. Sars-cov-2 delayed Tokyo 2020 olympics: Very recent advances in covid-19 detection, treatment, and vaccine development useful conducting the games in 2021. *Advances in Infectious Diseases*. 2020; 10(3): 56-66.
- [33] Shervani Z, Khan I, Qazi UY. COVID-19 vaccine. *Advances in Infectious Diseases*. 2020; 10(3): 195-210.
- [34] Shervani Z, Khan I, Khan T, Qazi UY. World's fastest supercomputer picks COVID-19 drug. *Advances in Infectious Diseases*. 2020; 10(3): 211-225.
- [35] Two-third of population surveyed in 11 states has coronavirus antibodies: ICMR serosurvey. [Internet] [cited July 28, 2021] The Times of India.
- [36] One in three Indians still vulnerable to COVID-19, says ICMR: findings of fourth serosurvey explained. [Internet] [cited July 22, 2021] Firstpost.
- [37] Seropositivity highest in Madhya Pradesh, lowest in Kerala, finds ICMR's national sero-survey. [Internet] [cited July 28, 2021] India Today.
- [38] 6th Delhi sero survey shows 97% prevalence of antibodies. [Internet] [cited November 4, 2021] Hindustan Times.
- [39] First phase of vaccination to start on January 16. [Internet] [cited January 9, 2021] The Hindu.