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Review Article

Community Section

Anti-SARS-CoV-2 Antibody Seroprevalence Surveys in India: An Insight into Current COVID-19 Pandemic Situation

SUDARSHAN RAMASWAMY[1], ARPIT ARORA[2], ADITYA ATHOTRA[3], MEERA DHURIA[4], ARTI BAHL[5], ANIL DIGAMBAR PATIL[6], SUDHIR KUMAR JAIN[7], SUJEET KUMAR SINGH[8]

ABSTRACT

Antibody test is used in seroprevalence surveys for Coronavirus Disease-2019 (COVID-19). Apart from estimating the proportion of population infected, they can help in drawing plenty of inferences about the extent, progress and course of the pandemic. They can potentially be helpful in planning and prioritising vaccine distribution by providing a broad overview into proportion of population immune to COVID-19 in a geographic area and also help in understanding the pockets of high or low seroprevalence. This review was conducted with an aim of compiling an updated and comprehensive information about the seroprevalence of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) antibody in various pockets of India in the year 2020, and thus to understand the current pandemic situation in the country. A total of 35 studies were identified through all resources and detailed review was carried out based on these studies. Additionally, indicators were devised to understand and compare the results. Results were further classified into states/Union Territories (UTs), districts, Sub-district regions. The study findings show that the anti SARS-CoV-2 antibodies seroprevalence estimates vary across different regions (states/UTs, districts, sub district regions) of India and can increase or in some instances decrease over the course of time. The study concludes by asserting the need for repeated seroprevalence surveys as well as follow-up studies for current pandemic surveillance.

Keywords: Herd immunity, Infection case ratio, Seroepidemiologic studies, Vaccination

INTRODUCTION

Ever since the announcement of the efficacy of few COVID-19 vaccines through the interim analysis of placebo-controlled phase III trials (mid phase), a sigh of relief and a ray of hope on moving back to normalcy from the current pandemic situation has been felt across the world. Nevertheless, even after approval of vaccines, one of the major challenges for public health experts remains the distribution of vaccines across the population throughout the world. As various countries are developing their vaccine introduction and national deployment plans for COVID-19, stress is laid upon introducing vaccination in phased manner by defining age-based, risk specific prioritisation of population subgroups [1]. COVID-19 vaccination rollout in India shall be a nuance operation and unique in its own way since it requires more extensive coverage than previously conducted vaccination drives such as “Pulse Polio Immunisation” or “Measles Rubella (MR) campaign” in which target group was a subset of population (under-5 children) unlike the COVID-19 vaccination program which demands much more extensive coverage across all age groups. However, providing vaccination on priority basis to those subgroups of population who are at high risk contacting infection (front line healthcare professionals) or mortality (persons over 60 years of age and persons between 45 and 59 years with comorbid conditions) is being considered [2].

Seroprevalence surveys can provide a broad overview into proportion of population immune/not immune to COVID-19 in that geographic area and also help in understanding the pockets of high or low seroprevalence, potentially helpful in planning and prioritising vaccine distribution. Secondly, effectiveness of any immunisation program in the general population after introduction of the vaccine not only depends on monitoring the efficacy and safety of the vaccine (phase 4 trials) but also depends upon immunisation coverage. Moreover, the knowledge of herd immunity threshold for COVID-19 vaccine is necessary for effective immunisation coverage. ‘herd immunity’, also known as ‘population immunity’, is a concept used for vaccination, in which a population can be protected from a certain virus if a threshold of vaccination is reached [3]. Based on the existing evidence from seroprevalence studies across the world, herd immunity threshold due to natural infection too is quite early to call [4]. Duration of persistence of immunity after natural infection/after single dose of vaccination and after multiple/booster doses shall also thus influence the effectiveness of immunisation program. Repeated seroprevalence surveys and follow-up studies, hence provide a parallel (may be earlier) insight into estimation of herd immunity threshold as well as antibody behaviour; both of which influence the effectiveness of immunisation programs [5].

The review aimed to compile an updated and comprehensive information about the seroprevalence of the anti SARS-CoV-2 antibody in various pockets of India in the year 2020, from the data available so far, and thus to understand the current pandemic situation in the country. The overall objective was aimed at providing a compiled base of reference for future analysis of serological studies, potentially helpful in planning, distribution, monitoring the effectiveness of COVID-19 vaccines in India.

LITERATURE SEARCH

The National Library of Medicine's PubMed database and Google scholar database was searched to identify potentially relevant publications. The search limits included all the seroprevalence studies conducted in India during the year 2020. The community-based (among general population) seroprevalence studies either published as articles in peer-reviewed journals or Government reports or whose results were presented by the States in COVID-19 review meetings conducted by Ministry of Health and Family Welfare (MoHFW), Government of India (GoI) during the year 2020 were included [Table/Fig-1] [10-38]. Studies done through samples exclusively taken from hospitals or among Healthcare Worker (HCWs) or from diagnostic laboratories were excluded.

As on December 20, 2020 the authors searched National Library of Medicine (NLM) database using the following terms “(Seroprevalence or Serosurvey) and (COVID-19 OR anti SARS-CoV2 or SARS-CoV2)

AND (India)". The search results showed 14 articles and three [10,21,32] among them fit the selection criteria. The authors also searched Google scholar database using the following terms "Seroprevalence", "India", "COVID-19" which resulted 703 articles and all the 13 studies that fit into the selection criteria were included. Unpublished data was also searched, available in public domain regarding various COVID-19 (anti SARS-CoV2 antibodies) seroprevalence surveys in India through google search [11,12,14,16,19,26-29,34-37]. The relevant data were collected through various state government websites of health and family welfare, official websites of organisations involved in seroprevalence surveys across the country, press briefings, media reports and sources from National Center for Disease Control (NCDC), Directorate General of Health Services (DGHS), MoHFW, Delhi staff attending the regular review meetings on COVID-19 by MoHFW.

Validity assessment was not done since the data consisted of different stages of studies (published articles, unpublished data, press reports etc.), samples belonged to different epidemiological distribution (time, place and person) and conducted during different phases of the pandemic. The data obtained from literature search was classified as published articles (peer-reviewed academic journals), government reports and by personalised communication from the NCDC. The authors found results of serological surveys from a total of 33 studies through all sources. Among them, 16 were from peer-reviewed journal articles (with 18 sets of data as data from Brehampur and Bhubaneshwar [16] included in one article and data from Delhi in August and September [19] taken from one article) [10-12,14,16,19,21,26-29,32,34-37], four were from government reports (with five sets of data as data from Haryana in August and October [20] included in one report) [18,20,31,33] and nine were from review meetings (with 10 sets of data as data for Punjab and Ludhiana [24] included in one meeting report) [Table/Fig-1] [13,15,17,22-25,30,38]. As all the serosurveys included were officially conducted by respective governments either directly or through partner agencies, and few of them yet to be published/under the process of publication in peer reviewed journals, alternatively newspaper articles were considered for knowing the estimated prevalence and sample size. Data obtained from all the studies were compiled in MS Excel and a detailed review was done.

Results have been grouped into six geographic zones of India according to the existing administrative "Zonal Councils" that were set up vide part-III of the States Reorganisation Act, 1956 [6]. Results were further classified into States/UTs, District, Subdistrict regions. An estimate of number of infections based on the projected population of the district/region (as per macrotrends website) [7] was made for all the studies. Infection Case Ratio (ICR), Case Fatality Rate (CFR) and Infection Fatality Rate (IFR) were also calculated. CFR and IFR were calculated based on the average time for seroconversion (14 days) and average time of death after infection (21 days) respectively [8,9].

C=Number of reported cases on (Mid-point of survey-14 days)

$$I=\frac{\text{Population of the district/region}\times\text{seroprevalance}}{100},\quad ICR=I/C$$

$$CFR=\frac{\text{Number of deaths reported on (Mid-point of survey-14 days)}}{\text{Number of cases reported on (Mid-point of survey-14 days)}}\times 100$$

$$IFR=\frac{\text{Number of deaths on (Mid-point of survey-7 days)}}{1}\times 100$$

- The number of expected infections (I) has been calculated based on the seroprevalence values based on the projected population of the district/region (as per macrotrends website) [7]. Intending to maintain uniformity and for comparison across the studies, calculation of infections for all the districts/states/towns has been done based on the 2011 census population data projected for 2020 (mid-year) acquired from a single website whose data source is United Nations - World Population Prospects [7].
- Mean time for seroconversion is 12-14 days for IgG after onset of symptoms for total antibody [8]. Hence, a 14-day gap is considered between the reporting of cases and the actual seroprevalence.
- Studies have shown that mean duration from onset of symptoms to death due to COVID-19 as 18 days [9]. Considering 2-3 days delay in reporting deaths, 21 days was conveniently used as the gap between case reporting and mortality (14+7 days).

Overall average for all the three parameters calculated has been compared with the two nationwide serosurvey results conducted by ICMR [10,11].

RESULTS

Central zone: In Indore, a serosurvey was conducted in the month of August with a sample size of 7,100. Stratified random sampling was used to collect the samples and Indian Council of Medical Research (ICMR)-Kavach IgG ELISA kits were used for detecting the presence of antiodies in the samples. The study was conducted for 15 days and collected samples from all 85 wards in the city. Overall weighted sero prevalence of 7.75% [12]. Adopting a similar sampling strategy, serosurvey was conducted in Bhopal in September where 7,976 samples were collected and the overall weighted sero prevalence of 18.02% was reported for the city [13]. On similar methodological lines, Jabalpur conducted a city-wide sero survey in the month of December. Out of the 9000 samples collected, 28.7% of the sample population showed positive antibody results [14].

A serosurvey was conducted in Uttar Pradesh during the month of September, in which 16,000 participants were tested. The samples were equally distributed among the top 11 districts with highest COVID-19 caseprevalence, from which 22.1% of the samples showed antibodies against the SARS-CoV-2 [15].

East zone: In Odisha, during the month of August, serosurveys were conducted in Berhampur and Bhubaneshwar with asample size of 2830 and 1320, respectively. Participants above 18 years were selected for the study. Twenty-five clusters were identified in each city based on population proportional to size. Multi-stage clustered sampling was used to identify the participants. The seroprevalence for Berhampur and Bhubaneshwar was found to be 31.30% and 5.15% respectively. Participants working in manufacturing sector were found to have higher seroprevalence for both, Bhubaneshwar (9.67%) and Berhampur (39.16%) [16,17].

Based on the study methodology adopted for serosurvey in August, another serosurvey was conducted in Bhubaneshwar in October. 1,403 samples were collected using a multi stage clustered sampling approach from 25 clusters in the city. A 50% of the samples showed positive results in the seropositivity tests [17].

North zone: Till date four serosurveys have been carried out and effectively completed in Delhi. First serosurvey was conducted in July, where 21,387 samples were collected and tested based on multi-staged systematic sampling approach. Samples were distributed across all the 11 districts based on proportional population [18,19]. The overall seroprevalence from the study was 23.48% [18]. Subsequently, in the next three serosurveys, a total of 15,046, 17,407 and 15,015 participants were tested during August, September, and October respectively [19]. The selection of participants in all three studies was through a multi-stage sampling design from all the 11 districts and 280 wards of the city, with two-stage allocation proportional to population-size. The households were selected via systematic random sampling, and individual participants were selected through the age-order procedure. The inclusion criteria of participants was age >5 years, residing in Delhi for at least the past six months and have not participated in previous

serological surveys. The seroprevalence was 28.45%, 25.10%, and 25.06%, respectively [19].

Two state-wide serosurveys were carried out in Haryana in August and October. Both the serosurveys covered all 22 districts of the state. In the first serosurvey, 18905 samples were collected and analysed using stratified multi-stage sampling approach. Samples were equally divided among all the 22 districts (850 per district) with 60% and 40% distribution of samples among rural and urban areas respectively for each district. All the participants were above 18 years of age. Overall seroprevalence for the state was 8% with huge district-wise variations. In the second study, 16,512 (720 per district) samples were tested. Overall seropositivity for the state during October was 14.8% [20].

In the Union Territory of Jammu and Kashmir, the first study carried out in July was restricted to Srinagar. A total of 2,906 persons aged >18 years were selected from hospital visitors across Srinagar District. The overall seroprevalence was found to be 3.6% [21]. Next serosurvey was conducted in October and all 10 districts of Kashmir were included. 6,200 people tested during the study and the results revealed a seroprevalence of 39% [22].

In Punjab, the first sero-survey was conducted across five containment zones during the month of August from which 27.7% of the sampled population (1250, 18 years of age) had developed antibodies against the virus [23]. The containment zones were selected on the basis of highest number of COVID-19 cases and the samples were equally divided. Another serosurvey was conducted across 12 districts of Punjab in November in which 4,678 samples were tested. Each district was given a sample size of 400 with equal distribution among urban and rural areas. The seroprevalance in urban areas was found to be 30.5%, while in rural areas it was 21%. The overall seroprevalence across the State was found to be 24.19% and the district of Ludhiana was found to have the highest overall seroprevalence of 54.6% (71.7% in urban areas) [24].

North-east zone: In a serosurvey conduced by an NGO in different districts of Assam during the month of September, 23.7% of the state's population was found to have been exposed to the SARS-CoV-2 virus. The districts were stratified into three categories high, medium and low risk, and 2,390 samples were collected for the study [25].

South zone: In a state-wide serosurvey carried out in Karnataka in the month of August, 46.7% of the population was found to have antibodies against the Sars-Cov-2 virus. The comparative study found that seroprevalence in rural areas was 44.1% and 53.8% in urban areas. Different sampling approaches were used for rural and urban areas. In case of urban areas, 21 Census Enumeration Blocks (CEBs) were chosen for each town via a simple random selection. Within each CEB, systematic random sampling was used to identify households for sample collection. However, in case of rural areas, households were first identified based on central street followed by systematic random sampling as in the case of urban areas. A total 1,374 samples were collected during the study froum 20 out of 30 districts in the state [26]. Another state-wide serosurvey was carried out in the month of September, which involved 16,416 participants aged ≥18 years across all the 30 districts. The population was stratified into three risk groups based on community exposure and vulnerability to COVID-19. All participants were subjected to simultaneous detection of SARS-CoV-2 IgG using a commercial ELISA kit, SARS-CoV-2 antigen using a Rapid Antigen Detection Test (RAT), and Reverse Transcription-Polymerase Chain Reaction (RT-PCR) for RNA detection. The overall seroprevalence in the state was found to be 27.3% [27].

A serosurvey was conducted during the month of July in Chennai involving 12,405 participants in which 18.40% of the total samples were found to have developed antibodies against the virus [28]. Another serosurvey was conduced in October in Tamil Nadu with 26,640 participants. The overall seroprevalence was found to be 31.6%, with Chennai showing a seroprevalence of 40.94% (26,135 samples) [29].

In Andra Pradesh, a state-wide serosurvey was carried out in August, with a sample population of 5000 for each of the 13 districts. A 19.7% of the population sampled were found to have developed antibodies against the virus. In case of urban areas, the seroprevalence was found to be 22.5%. In case of rural areas, 18.2% of the sample population was found to have developed immunity against the virus. In terms of gender, similar seropositivity was observed in case of females (19.9%) and males (19.5%) [30].

In a joint study, conduced by ICMR and National Institute of Nutrition in 3 districts of Telangana, 12.2% of the sampled population was found to have developed antibodies. Total 1,309 sample were collected for the study- 454 people in Jangaon, 433 in Kamareddy and 422 in Nalgonda. The highest seroprevalence was found in Jangaon district (18.2%) [31].

West zone: In Mumbai, two serosurveys were conducted in successive months of July and August respectively. In the study carried out in July, slum and nonslum communities from three wards-Matunga, Chembur West, and Dahisar—were identified for sample collection. Individuals over age 12 were eligible for the study. 6,904 participants (4,202 from slums and 2,702 from non-slums) were tested using representative sampling approach. The seroprevalence in slums (54.1%) was found to be 3 times higher than non-slums (16.1%). For the study carried out in August, 5,200 samples were analysed from the same three wards with no sampling carried out in active containment zones. The study estimated that 44.9% of the slum population and 17.5% of the non-slum population was exposed to the virus [32,33]. In Aurangabad, a study to identify seropreavalence was carried out across the district. Total sample size of 6,571 individuals above 18 years of age was selected. Samples from slums and non slums were taken based on population proportional to size. Estimated seropreavalence in the district was found to be 5.81% [34].

In a cross-sectional sero study carried out in five highest case incidence wards in the district of Pune, 51.5% of the sampled population showed immunity against the virus. Total of 1,664 participants were included in the study [35]. In the region of Pimpri-Chinchwad, a serosurvey on 5000 participants (all above 12 years of age) was conducted in October. The study used population proportionate cluster sampling for selection of participants. A 50, 80 and 70 clusters were chosen for slums, tenements, and housing societies respectively. The overall seropositivity for IgG antibodies was 35% [36].

Successive serosurveys were conducted in Ahmedabad during the months of July and August. In July, 30,000 samples were collected while in August 10,000 samples were taken and the seroprevalence in July was 17.6%, which jumped by 5.6% to 23.24% in August [37,38].

The overall average ICR from all studies listed was 81.42, as compared to 107.9 and 48.38 as calculated in [Table/Fig-1] for the nation-wide surveys conducted in May and August, respectively. Serosurvey conducted in Punjab during August resulted in the highest ICR at 494.35, and the one carried out in Pimpri, Maharashtra was found to have the lowest ICR of 7.1 [23,36]. Similarly, the overall average of CFR from all the studies included was 2.42% as compared to the nation-wide studies carried out by ICMR, at 2.8% and 1.9% for May and August, respectively [10,11]. Among the included studies, highest CFR of 6.5% was observed in Ahmedabad during the month of July, whereas the lowest CFR of 0.3% was recorded in Assam for the month of September [25,37]. The overall average IFR from all studies listed was 0.073%, as compared to 0.054% and 0.051% obtained from the nationwide surveys conducted in May and August,

respectively [Table/Fig-1] [10-38]. Aurangabad and Assam recorded the highest (0.310%) and lowest (0.006%) IFR, respectively [25,34].

A summary of all the studies described above is shown in [Table/Fig-1] [8-38]. It was noticed that seroprevalence was higher in urban areas as compared to rural areas in almost all the studies [10,11,20,27,29] which reported comparative assessment involving both sections. Similarly, in all studies [10,11,19,28,32,33] showing slum vs non-slum comparisions, it was noticed that seroprevalance was higher in slums/overcrowded areas than non-slum areas. There was no significant gender disparity in seroprevalence overall. The

Sr. No.	Author/Institution conducting the study	Source	Study site	Sample size	Sample population	Seroprevalence in %	Period	Number of infections as per seroprevalence estimate=I [7-9]	Infection-Case Ratio (ICR) [8,9]	Case Fatality Rate (CFR) in % [8,9]	Infection Fatality Rate (IFR) in % [8,9]
CENTRAL ZONE [6]											
1	Sakalle S et al., [12]	Peer-reviewed journal (GS)	Indore, MP	7100	General population	7.75	August	23,4,421	31.47	3.5	0.146
2	GMC Bhopal [13]	Review meetings*	Bhopal, MP	7976	General population	18.02	September	43,0,678	40.27	2.4	0.079
3	Ramaswamy S et al. [14]	Peer-reviewed journal (GS)	Jabalpur, MP	9000	General population	28.7	December	3, 54,870	31.41	1.5	0.010
4	KGMC Lucknow [15]	Review meetings*	Uttar Pradesh	16000	General population	22.1	September	5,11,66,146	217.03	1.4	0.009
EAST ZONE [6]											
5	Khan SMS et al. [16]	Peer-reviewed journal (GS)	Berhampur, Odhisha	2830	General population	31.3	August	1,27,704	66.51	1.6	0.032
6	Kshatri JS et al. [16]	Peer-reviewed journal (GS)	Bhubaneshwar II, Odhisha	1320	General population	5.15	August	59,895	9.21	0.4	0.067
7	RMRC Bhubaneshwar [17]	Review meetings*	Bhubaneshwar III, Odhisha	1403	General population	50	October	5,81,500	29.76	0.4	0.019
NORTH ZONE [6]											
8	NCDC, MoHFW [18]	Government report	Delhi-I	21387	General population (people aged >5 years)	23.48	July	71,12,327	79.2	3	0.049
9	Sharma N et al., [19]	Peer-reviewed journal (GS)	Delhi-II	15046	General population (>5 years) last survey participants excluded)	28.45	August	86,17,790	63.03	2.8	0.049
10	Sharma N et al., [19]	Peer-reviewed journal (GS)	Delhi-III	17,407	General population (>5 years) last survey participants excluded)	25.1	September	76,03,041	42.94	2.1	0.063
11	Sharma N et al., [19]	Peer-reviewed journal (GS)	Delhi IV	15015	General population (>5 years) last survey participants excluded)	25.06	October	75,90,924.6	41.62	1.9	0.078
12	NHM, Haryana [20]	Government report	Haryana-I	18905	General population	8	August	23,10,007	64.6	1.1	0.023
13	NHM, Haryana [20]	Government report	Haryana-II	16512	General population	14.8	October	42,73,513	32.9	1	0.024
14	Khan SMS et al., [21]	Peer-reviewed Journal (NLM)	Srinagar, J&K	2906	General population (people aged >18 years included)	3.6	July	57,096	105.93	2.3	0.086
15	GMC Srinagar [22]	Review meetings*	Kashmir, J&K	6200	General population	39	October	58,33,328	76.59	1.6	0.023
16	Government of Punjab[23]	Review meetings*	Punjab-I	1250	General population (Containment zones)	27.7	August	84,35,165	494.35	2.6	0.009
17	Government of Punjab [24]	Review meetings*	Punjab-II	4678	General population	24.19	November	73,66,304	54.98	3.1	0.061
18	Government of Punjab [24]	Review meetings*	Ludhiana, Punjab	400	General population	54.6	November	10,13,922	49.8	4	0.085
NORTH EAST ZONE [6]											
19	Srijanasom (NGO) and medicity Guwahati [25]	Review meetings* with NHM Assam	Assam	2390	General population	23.7	September	85,37,843	76.42	0.3	0.006

SOUTH ZONE [6]											
20	Mohanan M et al., [26]	Peer-reviewed journal (GS)	Karnataka-I	2912 house-holds	General population	46.7	August	3,24,97,126	251.36	1.7	0.012
21	Babu GR et al., [27]	Peer-reviewed journal (GS)	Karnataka-II	16416	Susceptible population (people aged >18 years included)	27.3	September	1,89,97,249	39.97	1.6	0.039
22	Selvaraju S et al., [28]	Peer-reviewed journal (GS)	Chennai, Tamil Nadu-I	12405	General population	18.4	July	20,18,664	26.92	2.7	0.099
23	Malani A et al., [29]	Peer-reviewed journal (GS)	Chennai, Tamil Nadu-II	26135 (for whole State)	General population	40.94	October	44,91,527	21.66	1.8	0.086
24	Malani A et al.[29]	Peer-reviewed journal (GS)	Tamil Nadu	26135	General population	31.6	October	35,43,668	34.07	1.59	0.047
25	Government of Andhra Pradesh[30]	Review meetings*	Andhra Pradesh	65000	General population	19.7	August	1,80,68,296	120.25	0.9	0.014
26	ICMR-NIN[31]	Government report	Telangana	1309	General population	12.2	May-August	48,02,253	37.61	0.6	0.02
WEST ZONE [6]											
27	Malani A et al., [32]	Peer-reviewed journal (NLM)	Mumbai-I, Maharashtra	6904	General population	33.56#	July	68,49,931	104.85	5.7	0.08
28	BMC, Mumbai [33]	Government report	Mumbai-II, Maharashtra	5200	General population	28.8#	August	58,78,368	48.93	5.6	0.131
29	Dixit D et al., [34]	Peer-reviewed journal (GS)	Aurangabad, Maharashtra	6571	General population	5.81	August	1,84,000	13.13	3.1	0.31
30	Ghose A et al., [35]	Peer-reviewed journal (GS)	Pune, Maharashtra	1664	General population	51.5	July-August	34,13,935	37.14	2.4	0.064
31	Banerjee A et al., [36]	Peer-reviewed journal (GS)	Pimpri, Maharashtra	5000	General population	35	October	6,04,692	7.1	1.8	0.257
32	Prakash O et al., [37]	Peer-reviewed journal (GS)	Ahmedabad-1, Gujarat	30000	General population	17.6	July	14,24,909	67.44	6.5	0.107
33	Ahemdabad municipal corporation. [38]	Review meetings*	Ahmedabad-2, Gujarat	10000	General population	23.4	August	18,85,909	70.73	5.7	0.088
Average from all the above studies									81.42	2.42	0.073
34	Murhekar MV et al., [10]	Peer-reviewed journal (NLM)	INDIA , ICMR-I	28000	General population	0.73	May-June	1,00,74,032	107.9	2.8	0.054
35	Murhekar M et al., [11]	Peer-reviewed journal (GS)	INDIA, ICMR-II	29000	General population	7.1	August	9,79,80,311	48.38	1.9	0.051

[Table/Fig-1]: Summary of population-based COVID-19 seroprevalence studies in India during the year 2020.
Peer-reviewed journal (GS)=Google Scholar, (NLM)=PubMed National Library of Medicine Catalogue; *National Center for Disease Control (NCDC); Delhi has been working for Ministry of Health and Family Welfare; GOI and is supporting various States/State Governments on epidemiological surveillance related activities throughout the course of COVID-19 pandemic in India. In the due course; details of several COVID-19 serological studies were presented to NCDC during multiple official review meetings; • # Average seroprevalance for Mumbai is calculated based on the values obtained from Slum and Non-Slum populations. Weightage was given 40:60 for slum: non-slum based on the 2011 census data where Mumbai had 42% population dwelling in slums. Considering 2% attrition during lockdown due to migration, a ratio of 40:60 was used

seroprevalence across age-groups was variable across the studies but the age group between 40-60 years was noticed to be the highest seroprevalent age group in many studies.

DISCUSSION

Seroprevalence: This review shows that seroprevalence estimates of the anti SARS-CoV-2 antibodies vary across different regions of India (states/UTs, districts, sub district regions) and increased over the course of time. For instance, serial studies conducted in Bhubaneshwar [16,17], Ahmedabad [38], Chennai [28,29] the two ICMR nationwide surveys [10,11] show an increasing trend. However, some instances have shown a decreasing trend in serial studies such as in Punjab [23,24], Karnataka [26,27], Mumbai [32,33]. Repeated serosurveys in Delhi [18,19] have shown a variable pattern and more or less a consistent trend over the period of time in the year 2020.

While a positive trend (increase in seroprevalence over time) could be attributed to the spread of the disease, witnessing a negative trend (decrease in seroprevalence over time) have raised several questions. Serial serosurveys in Delhi give a good picture of both these phenomena happening simultaneously. One of the probable explanations for a negative trend could be fading away of antibodies over the course of time. It is consistent with several serial seroprevalence studies and longitudinal follow-up studies which have shown declining prevalence of anti SARS-CoV-2 antibody detection over time [4,5,39-42]. A longitudinal follow-up study conducted by Oxford university during the early phases of the COVID-19 pandemic concludes that IgG antibody levels to SARS-CoV-2 nucleocapsid wane within months, much faster in younger adults and those without symptoms. The study also estimates that the mean antibody half-life to be 85 days [43]. Additionally, case reports suggestive of possibility of clinically recovered patients

failing to be seropositive, occasional reports of COVID-19 reinfection and with the evidences of virus mutating into more severe forms (variants of concern - increasing transmission/virulence/resistance to neutralising antibodies) suggest that the pandemic is still far from being over [44-47]. Hence, it is very essential to aggressively re-emphasise the importance of basic COVID-19 appropriate preventive measures (physical distancing, wearing masks, maintenance of respiratory etiquette, hand sanitisation, consumption of nutritious food, prevention of non-communicable diseases through lifestyle modification and medication adherence) and counter the risk-communication fatigue in the community [48]. There is a need to focus on implementing preventable and modifiable risk factors (as mentioned above), simultaneously understanding the changes in disease dynamics expected as a result of non-modifiable factors pertaining to the agent (e.g., mutations) and host (e.g., duration of antibody response). Hence, ensuring the inculcation of COVID-19 appropriate behaviour, attitude and perception is to be highly recommended universally, irrespective of prior infection. Repeated seroprevalence surveys/ follow-up studies are essential for pandemic situation update, regular monitoring and surveillance is necessary for identification of any changes indynamics of the current pandemic.

Seroprevalence and related indicators: Highly variable estimates of ICR/CFR/IFR were noticed among different seroprevalence surveys and also as compared to the national surveys or the overall average obtained by various listed surveys. This difference can be attributed to the fact that the studies under consideration are not a true representation of the socio-demographic landscape of India. The studies are from various pockets across India and represent different timelines/phases of the pandemic. High ICR (number of infections per case) implies that the proportions of actual infections being detected as cases are being less. Although detection of all the asymptomatic cases could be a very tough task to ask for, improving the proportion of cases detected through contact tracing shall reduce/slower the spread of COVID-19 disease. Having high ICR also can be reflected as high CFR. While high ICR/CFR imply that case detection and extent of contact tracing needs improvement, a higher CFR/IFR additionally stresses upon the need to enhance the healthcare infrastructure and manpower. Continuous serial monitoring of these indicators are recommended until the pandemic settles down because they can give preliminary indications of any potential influences requiring change in pandemic response activities in the country.

Seroprevalence surveys and vaccination: Though Phase 3 vaccine trials show promising results, vaccine effectiveness in general population is yet to be seen (Phase 4 trials) [49]. Apart from effectiveness, it is important to know the herd immunity threshold for vaccination coverage. Seroprevalence surveys so far have resulted in no clear-cut idea about herd immunity. Hopes of natural herd immunity at seroprevalence level as high as 66% estimate after the 1st wave of COVID-19 in Manaus, Brazil has resulted in disappointment due to resurgence of the virus observed as a second wave of COVID-19 cases [4,5,50]. Such instances have raised questions about the extent of vaccination coverage needed for obtaining herd immunity status. Published literature suggests that duration of anti SARS-CoV-2 antibodies last much shorter in India [51].

All these factors suggest that continuous serosurveillance is very much essential during the phase of vaccination in India as well. Hence, one of the biggest challenges lying ahead for public health experts is amplifying vaccination coverage and simultaneously educating people on a large scale for continuing COVID-19 appropriate behaviours even during post-vaccination phase; until a clear-cut picture on effectiveness of seroconversion is obtained through longitudinal follow-up studies. Nonetheless, as COVID-19 vaccine is provided on a voluntary basis, good vaccination coverage in a quick succession can be established only through an effective participation from the community. Since the vaccination program is already being implemented in a full-fledged manner, a continuous sensitisation of the community addressing the issues of COVID-19 vaccination intent, perceptions and reasons for not getting vaccinated/vaccine hesitancy is highly recommended.

Limitation(s)

The population used to calculate total number of infections and thus ICR or IFR, do not use the exact population used while calculating the sample size of respective studies. For maintaining uniformity across different studies, calculations have been done based on the projected population for 2020 acquired from a single website.

CONCLUSION(S)

It is recommended to intensify serological studies and simultaneously apply the knowledge and understanding thus obtained for faster recovery from the situation of debacle we are currently in. Continuous seroprevalence studies and longitudinal follow-up studies have to be done in purview of understanding the various facets of this disease such as the extent of disease spread among the population, herd immunity threshold levels of COVID-19, pattern of serological response to infection, duration of antibody stay in the body, indications of any potential variations of concern (through seroprevalence related indicators), response to vaccination and associated aspects. Furthermore, seroprevalence studies undertaken particularly on Indian population shall be of greater importance as genetic factors too can possibly influence these components.

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PARTICULARS OF CONTRIBUTORS:
1. Consultant (NO-A)-Health Emergencies, World Health Organisation, WCO, New Delhi, India. (Posted in Department of Epidemiology, NCDC) .
2. Research Scholar, Department of Centre for Technology Alternatives for Rural Areas, IIT Bombay, Mumbai, Maharashtra, India.
3. Statistical Officer, Statistical Monitoring and Evaluation Cell, National Centre for Disease Control (NCDC), New Delhi, India.
4. Deputy Director, Department of Epidemiology, National Centre for Disease Control (NCDC), New Delhi, India.
5. Joint Director, Department of Epidemiology, National Centre for Disease Control (NCDC), New Delhi, India.
6. Additional Director and Head, Statistical Monitoring and Evaluation Cell, National Centre for Disease Control (NCDC), New Delhi, India.
7. Additional Director and Head, Department of Epidemiology, National Centre for Disease Control (NCDC), New Delhi, India.
8. Director, National Centre for Disease Control (NCDC), New Delhi, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Meera Dhuria,
Deputy Director, Department of Epidemiology, National Centre for Disease Control,
22, Sham Nath Marg, Delhi, India.
E-mail: meera.dhuria@gov.in

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