Original article

Assessment the level of Immunity against COVID-19 among Uttar

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Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS CoV 2) is the virus that causes COVID-19 (coronavirus disease 2019), the respiratory illness responsible for the COVID-19 pandemic. It has created a devastating effect on humanity with social and economic depression. Europe and America were the hardest hit continents. India has also lost lives, making the country fourth most deadly worldwide. However, the infection and death rate per million and the case fatality ratio in Uttar Pradesh were substantially lower than in many States in India. Several factors have been proposed including genetics. One of the important facts is that a large chunk of Uttar Pradesh population is asymptomatic to the SARS-CoV-2 infection. Thus, the real infection in Uttar Pradesh is much higher than the reported number of cases. Therefore, the majority of people are already immune in the states. To understand the dynamics of real infection as well as the level of immunity against SARS-CoV-2, we have performed antibody testing (serosurveillance) in the urban region of ten districts in Uttar Pradesh in our survey, the prevalence frequency varied between 0.01-0.48, suggesting high variability of viral transmission between District. We also found out that the cases reported by the government were several folds lower than the real incidence of infection. This discrepancy is mainly driven by the higher number of asymptomatic cases. Overall, we suggest that with the high level of immunity developed against SARS-CoV-2 in the majority of the districts, the case fatality rate of second wave in India will be minor than first wave.

Keywords: Antibody, Coronavirus, India, Seroprevalence, Herd immunity

Introduction

SARS-CoV-2 produces clinical symptoms that include fever, dry cough, sore throat, dyspnea, headache, pneumonia with potentially progressive respiratory failure owing to alveolar damage, and even death.The number of people who died due to infection of this virus around the globe has also crossed the mark of 2 million (Dong et al., 2020). Before the roll-out of vaccination recently, it was highly challenging for a nation to stop the spread of this virus. Several of the standard precautionary measures, e.g. strict lockdown, the use of masks, frequent hand hygiene, social distancing, contact tracing and quarantine have been applied widely (Jung et al., 2020; Rodriguez-Palacios et al., 2020). Even so, virtually no country is yet able to declare itself completely free from the virus. Initially, herd immunity was also considered and widely discussed (Randolph and Barreiro, 2020; Slot et al., 2020).

Herd immunity against the SARS-CoV-2 is one of the highly debated topics (Anderson and May, 1985; Bock et al., 2020; Frederiksen et al., 2020; Jung et al., 2020; Kwok et al., 2020; Neagu, 2020). During a pandemic, when approximately 70% of the population get infected and develop antibodies against the pathogen, herd immunity should theoretically be attained. This barrier of immunity blocks

the virus and adds passive immunity to non-infected people. However, due to the high fatality rate of SARS-CoV-2 infection, nearly all countries did not adopt this strategy.

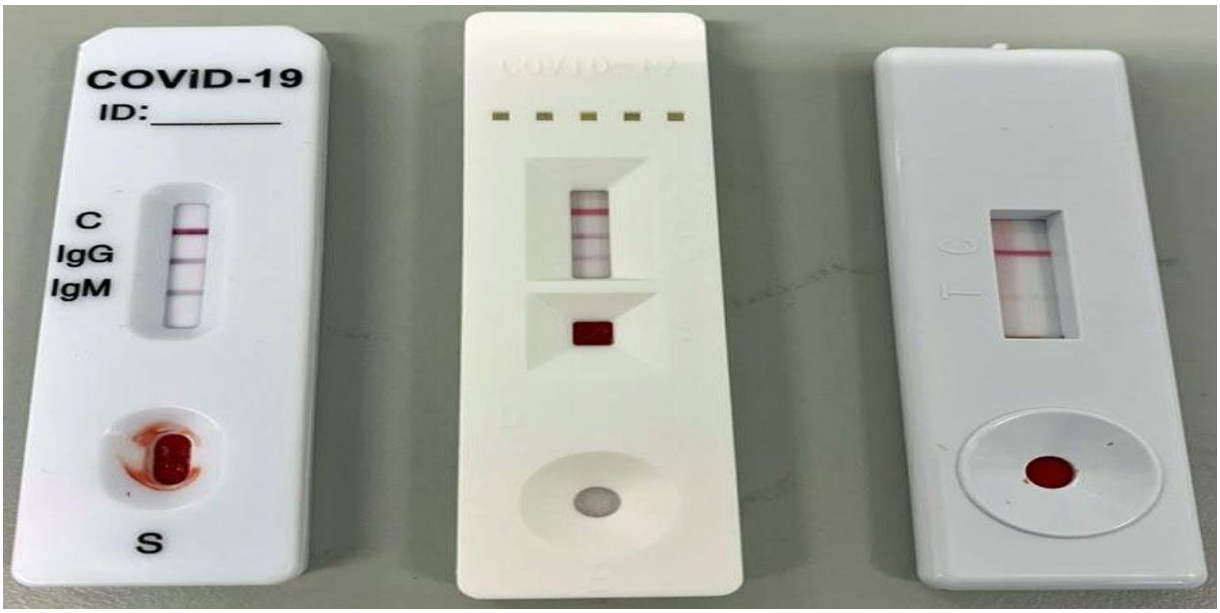
The model of herd immunity is very similar to the positive selection (or selective sweep), a term often used in the genomic studies (Sabeti et al., 2002; Voight et al., 2006). Similarly, we can also relate hard sweep and soft sweep terminology (Pritchard et al., 2010), for a soft and hard herd immunity. With the exclusion of hard herd immunity, the alternate option was to obtain the soft herd immunity with the strict use of defensive procedures. Protective measures like strict lockdown, the use of masks, frequent hand hygiene and social distancing have significantly reduced the effective infections and overburden to the emergency services (Aleta et al., 2020; West et al., 2020). Also with efficacious contact tracing and quarantine, soft herd immunity may be achieved over time (Aleta et al., 2020).

From the first case in India on 27th Jan 2020, now the total cases have surpassed >10 million with >0.15 million fatalities (Coronavirus in India: Latest Map and Case Count). Although still the new number of cases tallies at between 10-15,000 per day, Uttar Pradesh has followed a perfect bell-shaped curve with a well-defined peak in September 2020. Several studies have pinpointed that the real number of infected people in a population are several fold higher than the reported cases (Aspelund et al., 2020; Böhning et al., 2020; Ivorra et al., 2020; Mukhopadhyay and Chakraborty, 2020; Pedersen and Meneghini, 2020; Shaman, 2020). In addition, a large number of asymptomatic people add another layer of complexity, as has been seen in the case of India . Most studies relied upon mathematical modelling, which may not show the real picture of COVID-19 in Uttar Pradesh Random antibody testing in a population is one of the procedures to obtain a real-time picture of the developed immunity. Thus, to understand the COVID-19 dynamics in India, we have performed real-time antibody testing on urban populations from ten districts of Uttar Pradesh. The aim was to estimate the level of immunity against COVID-19 among estimate the level of immunity against COVID-19 among urban street vendors.

Materials and Methods

Since most of the COVID-19 cases in Uttar pradesh were concentrated on urban areas, we concentrated on urban populations in our survey. During the month of September- April 2021, we randomly surveyed healthy working individuals who have neither been diagnosed with COVID-19, nor had been sick with any associated symptom in the recent past. Moreover, we excluded those individuals in our survey whose family members have ever been diagnosed with the COVID-19 in the past. Our focus was to screen people from urban vendor group who are relatively more exposed in society, e.g. roadside workers, roadside fruit-vegetable sellers, rikshaw pullers, autorickshaw drivers, milkmen, hawkers etc. With these stringent criteria, we screened unrelated people who have not lived together. Informed consent were obtained from all the participants. Study was approved by the ethical committee of Banaras Hindu University, Varanasi, India.

We used CoviscreenTM kit, kindly provided by Biosense Technologies, India to screen the individuals for the presence of antibodies. This kit detects the total antibodies (IgM+IgA+IgG) present in the blood. We followed the manufacturers protocol for detection. A sample test for positive and negative samples. **Figure 1A.** The detection of antibodies by the CoviscreenTM kit. The kit produces one and two bands in case of Antibody negative and positive persons respectively.



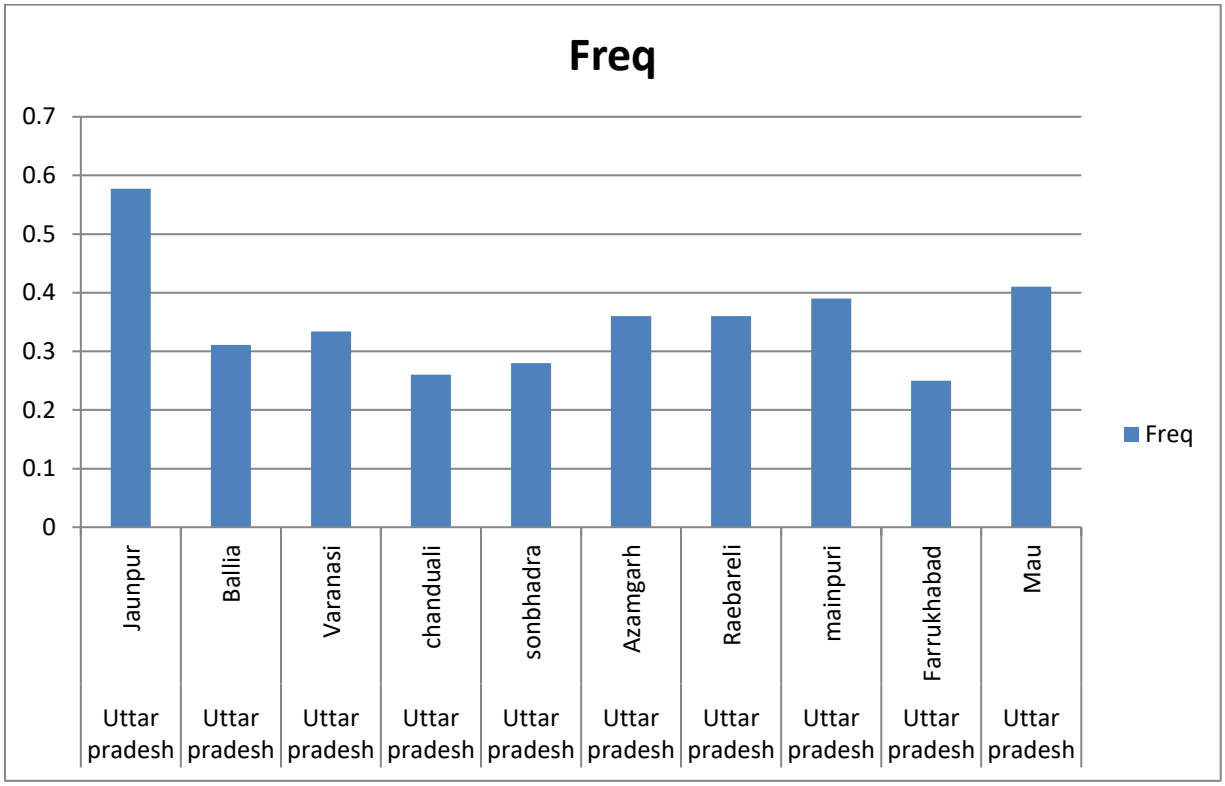
The frequency of antibody positive individuals were calculated in each of the districts surveyed (Table 1). The frequency bar plot of each district was drawn with 95% CI (Figure 1c). District-wise population census data were extracted from the 2011 census of India (Census of India WebsiteJ: Office of the Registrar General & Census Commissioner, India). Numbers of reported cases in each district were recorded from the Covid India tracker (Coronavirus in India: Latest Map and Case Count). This study has been approved by the Institutional Ethical Committee of Banaras Hindu University, Varanasi, India.

Results and Discussion

In our survey, geographically we have covered districts from, Eastern area of Uttar Pradesh, ten districts were surveyed in Uttar Pradesh,. Our seroprevalence survey in ten districts shown a high level of variability between regions **(Fig. 1b).** The minimum proportion of antibody- positive people was observed in chanduali district of Uttar Pradesh, whereas the maximum proportion of antibody-positive individuals was found in jaunpur district of Uttar Pradesh state (Figure 1b and Table 1). The mean prevalence among studied districts was 0.306 (95%CI 0.287-0.325). The high prevalence of antibodies in many of the districts suggests that soft herd immunity in India is well underway. The frequency of antibody-positive people is sporadic, however, with regions like eastern Uttar Pradesh showing a largely uniform seroprevalence **(Figs. 1b).** The mean value in this region was found to be 0.41 (95%CI 0.38-0.44). Major districts of this region like Varanasi, Jaunpur, Azamgarh and mainpuri all had a frequency of >0.36 prevalence. The variation among districts suggests that the level of virus spread among districts of Uttar Pradesh is asymmetrical. The low prevalence regions may hit by another wave.

Notably, all the participants in this study were found to be asymptomatic, they did not know that they ever had COVID-19. This suggests that a large proportion of the Uttar Pradesh population is asymptomatic against SARS-CoV-2 infection. Indeed, there might be several known and unknown reasons behind this phenomenon. However the prevalence of the rs2285666-associated haplotype (Srivastava et al., 2020) and the fact that ~65% of the Indian population is 35 years of age or younger are two highly likely explanations. In order to understand the magnitude of unreported cases, we have compared the frequency of government-reported cases with the frequency of antibody-positive cases. All of the districts showed higher seroprevalence than the reported cases **(Table 1).** The mean value of studied districts was 17 times (95% CI 13-22) higher than the government reported cases. Similar with the frequency dissimilarities, in a state-wise comparison, we observed substantial differences, Interestingly, we found out that cases reported by the government were highly correlated with the

urban census (two tailed p<0.0001), whereas we did not find any significant correlation between antibody-positive frequency with the urban census or government-reported cases.



As our result suggests that the number of real infections in India is several folds higher than the government-reported cases, we may reconsider the case fatality ratio CFR). The present case fatality ratio of India (1.44) is significantly lower (two tailed p value <0.0001) than the global average (2.15). Considering our result, which shows a far greater number of real infected people, the actual case fatality ratio of India is at least 17 times lower **(Table 1).** Table 1. The detailed districtwise data of seroprevalence. Frequency of Government cases has been calculated by number of reported cases/urban census. Number of times were calculated by dividing seroprevalence with frequency of Government reported cases.

State	District	Months	N	Antibody	Freq	Fre(Gov)	Case(Gov)	Urban census	Time
Uttar pradesh	Jaunpur	Sept 2020-feb 2020	456	263	0.577	0.019	6697	347000	22.9
Uttar pradesh	Ballia	Nov 2020-feb 2020	183	57	0.311	0.044	5346	121000	11
Uttar pradesh	Varanasi	Sept 2020-feb 2020	540	180	0.334	0.012	23360	2000000	35
Uttar pradesh	chanduali	Mar-20	50	13	0.26	0.19	6796	35600	22.9
Uttar pradesh	sonbhadra	Mar-20	60	17	0.28	0.025	72676	2817000	13
Uttar pradesh	Azamgarh	Apr-20	50	18	0.36	0.6992	43700	625000	5.1
Uttar pradesh	Raebareli	Feb-20	100	36	0.36	0.012	2376	191000	42
Uttar pradesh	mainpuri	Jan2020-march202	187	74	0.39	0.01	1574	150000	22
Uttar pradesh	Farrukhabad	Jan2020-march202	55	14	0.25	0.08	24615	276000	15
Uttar pradesh	Mau	Apr-20	80	33	0.41	0.017	3452	200000	6.3

Our observation at the ten districts of Uttar Pradesh indicates a sporadic high level of immunity among people who are highly contagious as well as exposed. Since our focus was on people who are more prone to receive as well as spread infection, our result indicates that a strong level of immunity wall has already come into effect. In this apparently unfolding scenario, it is likely that most of the hotspots are saturated with the immune people. The projected second wave may appear possibly due to new hotspots as well as more contagious new virus strains, however with the large number of immune people the impact of second wave will be moderate and sporadic than the first wave. This may

substantially reduce the case fatality ratio in second wave than the first wave.

In summary, for the first time we have used a novel approach to estimate the developed level of immunity against SARS-CoV-2 among the exposed populations of ten districts. These results strongly indicate that soft herd immunity is already in force in several of the Uttar Pradesh. We observed that on an average every third street vendor in the majority of the districts studied have developed antibodies against SARS- CoV-2. The number of asymptomatic cases in India is much higher than expected. Overall, we suggest that with the high level of immunity developed against SARS-CoV-2 in the majority of districts, it is unlikely to have a higher case fatality rate during second wave in India.

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