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Seroprevalence and infection attack rate of COVID-19 in Indian cities



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ABSTRACT

Objectives: Serological surveys were used to infer the infection attack rate in different populations. The sensitivity of the testing assay, Abbott, drops fast over time since infection which makes the serological data difficult to interpret. In this work, we aim to solve this issue.

Methods: We collect longitudinal serological data of Abbott to construct a sensitive decay function. We use the reported COVID-19 deaths to infer the infections, and use the decay function to simulate the seroprevalence and match to the reported seroprevalence in 12 Indian cities.

Results: Our model simulated seroprevalence matchs the reported seroprevalence in most of the 12 Indian cities. We obtain reasonable infection attack rate and infection fatality rate for most of the 12 Indian cities.

Conclusions: Using both reported COVID-19 deaths data and serological survey data, we infer the infection attack rate and infection fatality rate with increased confidence.

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1. Introduction

The COVID-19 pandemic has caused tremendous impact globally. The situation in terms of reported cases and deaths were low in the year 2020 in India. It was once claimed that the control in India was a success until a major second wave hit the country and caused large number of mortalities. But the reported deaths per capita are still relatively low compared to other developed countries. Velumani et al. (Velumani et al., 2021) studied seroprevalence in 12 Indian cities from July to December 2020. Their result showed two distinct patterns: a wave pattern, e.g., Mumbai and Pune, and a monotone increasing pattern,

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e.g. Delhi and others. These patterns were driven by the underlying COVID-19 pandemic in each city. However, the other key factor is the use of multiple brands of antibody testing machines (or assays): in particular Abbott and non-Abbott, e.g., Roche. Abbott and Roche are widely used serological testing devices in the market. The method of Abbott SARS-CoV-2 IgG assay is acridinium-labelled anti-human IgG. Roche used ruthenium-labelled and biotin-conjugated N protein to perform the Anti-SARS-CoV total antibody assay. Velumani et al. (Velumani et al., 2021) highlighted that two machines were used in this study, without specifying which city used which one. Presumably, the Abbott was used in these wave-pattern cities while Roche was in others (we explain the reason later). The two machines have very different 'decay rates' as found in (Muecksch et al., 2021), Fig. 1 shows a comparison of the sensitivities of Abbott vs Roche.

We observed that Abbott showed a very rapid drop in sensitivity over time for RT-PCR confirmed infections after RT-PCR confirmation (or onset of symptom for symptomatic cases after RT-PCR confirmation). While the sensitivity of Roche is stable. Thus, the seroprevalence obtained with Roche would be much closer to the infection attack rate (IAR, defined as the cumulative proportion of the infected population), which shows a monotone increasing pattern. Since the antibody level of infected individual will gradually wane over time which causes the sensitivity of the testing to drop (an infected person became seronegative), the seroprevalence will be lower than the IAR, and this is very evident with Abbott than Roche. We first estimated the sensitivity decay Backspace function of Abbott based on publicly available data of Abbott. Then we collected reported COVID-19 deaths and serological studies from 12 Indian cities. To connect the two sources of data, we used the independently estimated sensitivity decay function of Abbott to reconstruct the IAR and the seroprevalence simultaneously in 12 Indian cities. We found that our approach works well in most cities where Abbott was likely used and failed in a few cities where non-Abbott was likely used. Since we combined two sources of data, our inference on the IAR should be of higher confidence than that via using a single source of data.

2. Material and methods

2.1. Data

COVID-19 deaths data were obtained from https://api.covid19india.org. Serological survey data for 12 Indian cities were obtained from (Velumani et al., 2021). A serological survey is usually carried out to investigate the prevalence of the size of an epidemic (population infected) in a given population by identifying the presence of specific antibodies used against the virus (Anand et al., 2021; George, Raja Inbaraj, Chandrasingh, & de Witte, 2021; Inbaraj, George, and Chandrasingh 2021; Murhekar et al., 2020; Murhekar, Bhatnagar, Selvaraju, et al., 2021; Murhekar, Bhatnagar, Thangaraj, et al., 2021; Velumani et al., 2021).

2.2. Method

2.2.1. Sensitivity decay of Abbott

To quantify the sensitivity decay of Abbott, we collected data from several independent studies (Maine et al., 2020; Muecksch et al., 2021; Eberhardt et al., 2021; Kahre et al., 2021; Harris, Whitaker, & Andrews, 2021), pooled data together (see

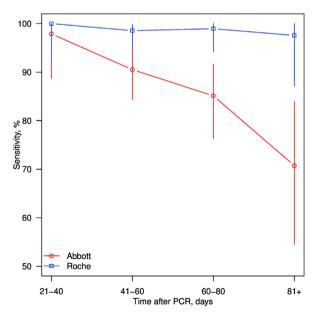


Fig. 1. A comparison of sensitivities of Abbott vs Roche over time. Data from (Muecksch et al., 2021). The sensitivity of Abbott drops faster over time.

Fig. 2a), and fitted a modified Gamma distribution function (which has a maximum value of 1, thus not a distribution function anymore) to the data to quantify the drop rate (see Fig. 2b). Thus, $f(t) = Gamma(t, \alpha, \beta)$. Hence, we found the best estimates $\alpha = 0.165$, $\beta = 0.012$.

2.2.2. The relationship between COVID-19 deaths and seroprevalence

Following (He, Fan, Wang, Li, & Peng, 2021, p. 21254281), we denoted the daily COVID-19 seroprevalence as p (proportion of population showing seropositive/antibody positive at a given day), daily sero-conversion as p^+ (seronegative individual turns seropositive), daily seroreversion as p^- (seropositive individual turns seronegative due to antibody waning), then we had the following equation:

$$p[T] = p[T-1] + p^+$$
 [in the last 24 hours] $-p^-$ [in the last 24 hours]

Assuming initially all these are zero, this can be written as

$$p(T) = \sum_{0}^{T} p^{+} - \sum_{0}^{T} p^{-}$$

Denote f(s) as the sensitivity decay function which is given in Fig. 2b.

$$p(T) = \int_{0}^{T} c(t)f(T-t) / Ndt$$

i.e., the convolution (here we rewrite the summation in the above equation into integral fashion) between c(t) and f(s), where c(t) is the time series of daily new cases, N is the size of the population. But, typically c(t) is not very reliable due to time-varying testing policy and testing effort and a significant amount of asymptomatic cases. Nonetheless, the data of daily COVID-19 deaths are available (by law in many regions) and relatively reliable than reported cases. We denoted r as the infection fatality ratio (IFR). Thus, the daily new cases are roughly given as c(t) = d(t+14)/r. We assumed a delay between date of death and date of case confirmation (ie, roughly symptom onset for symptomatic case) at 14 days. The seroprevalence on day T is given:

$$p(T) = \int_{0}^{T} r^{-1}d(t+14)f(T-t) / Ndt$$

We used the black curve in Fig. 2b as f(t) for Abbott. When f(t) = 1, p(T) = IAR(T), the infection attack rate is:

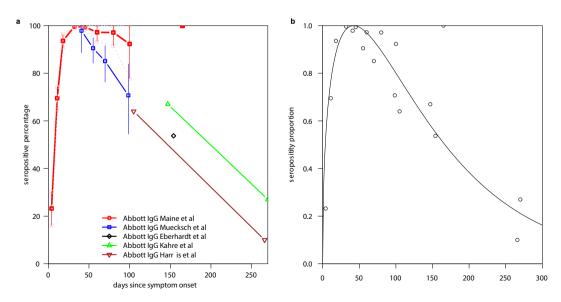


Fig. 2. Abbott sensitivity as a function of time after symptom onset for a group of PCR positive patients (panel a). We assume the date of symptom onset and the date of RT-PCR confirmation are close. We fit a model (see main text) to the observed data (panel b).

$$IAR(T) = \int_{0}^{T} r^{-1}d(t+14) / Ndt$$

Thus given f(s) and death data, we can get p(t) and IAR(t) easily if r is known. However, r estimates vary in previous studies, across locations and rely on the efforts of COVID-19 cases and deaths reporting. We argued that we may estimate r by matching p(t) to reported seroprevalences at different time points. If the matching is acceptable, then we may accept the reported seroprevalences (given that it was Abbott based), and we immediately obtained the IAR and r. We proposed the following approach to match p(t): we calculated the sum of squared errors (SSE) between p(t) and reported seroprevalence on six data points from July to Dec 2020 for a range of r, and chose the r which attains the smallest SSE.

3. Results

Fig. 3 and Table 1 showed the main results, where we applied our method to 12 large Indian cities. Since we did not know the IFR, we aligned the reconstructed seroprevalence (blue dashed curve) and serological survey (black curve with circles) using the approach given in Method; this alignment will yield an IFR r, which is applied to the whole reconstructed seroprevalence and the IAR curve (red curve). The reconstructed and observed seroprevalence matched reasonably well for most cities, where Abbott was likely used for most of the period. This works fine for most cities except for a few cities, e.g., Ahmedabad. In Ahmedabad, the serological survey went up faster than the increase in IAR. Thus, some mechanism unknown

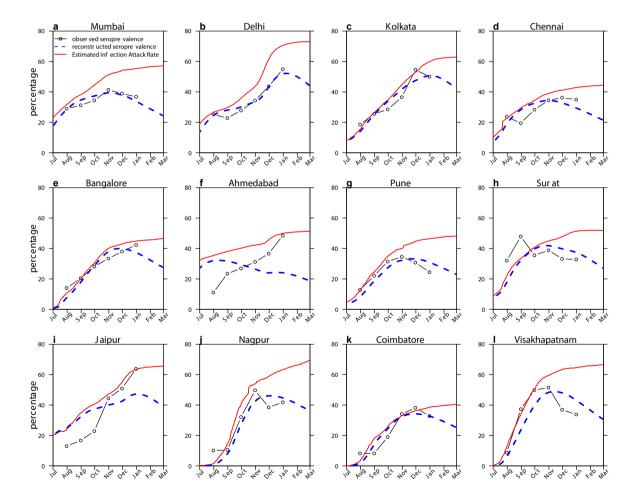


Fig. 3. Simulated attack rate (red curve) and seroprevalence (blue dashed curve) over time compared with serological surveys (black curve with circles) in 12 Indian cities (Velumani et al., 2021). The attack rate (AR) is a monotone-increase function of time given its definition. The seroprevalence is lower than the AR due to assay sensitivity which is less than 100% and sensitivity decay over time. We aligned the reconstructed seroprevalence and serological survey to yield an IFR which is applied to both the reconstructed seroprevalence curve and the AR curve.

Table 1Summary of estimates of infection attack rate and seroprevalence for 12 Indian cities.

City	Population (million)	Total reported COVID-19 deaths by Mar 1, 2021	Infection Attack Rate by Mar 1, 2021 (%)	Seroprevalence under Abbott on Mar 1, 2021 (%)	Estimated Infection Fatality Rate by Mar 1, 2021 (%)
Mumbai	18.4	11475	58.02	24.42	0.11
Delhi	16.3	10910	74.91	44.15	0.09
Kolkata	14.1	3101	72.77	42.22	0.03
Chennai	8.7	4150	47.77	21.56	0.1
Bangalore	8.5	4639	51.07	27.67	0.11
Ahmedabad	6.4	2313	49.51	18.8	0.07
Pune	5.1	8062	44.59	23.02	0.35
Surat	4.6	977	57.93	27.13	0.04
Jaipur	3.1	519	75.23	39.14	0.02
Nagpur	2.5	3521	60	36.61	0.23
Coimbatore	2.2	683	44.26	25.27	0.07
Visakhapatnan	n 1.7	567	59.41	30.68	0.06

might occur (e.g. non-Abbott or inconsistence assay or inconsistence in death reports) which affected the serological survey or led to dramatic changing in COVID-19 death reporting process.

In our method, we assumed that the reported COVID-19 deaths accurately reflected the attack rate subject to a constant IFR. This could fail if the death reporting effort dramatically changed or the intrinsic IFR changed (likely due to the emergence of new variants). The reconstructed seroprevalence successfully matched the reported serological surveys in Mumbai, Delhi, Chennai, and Coimbatore. The reconstructed seroprevalence also successfully matched the *trend* of serological surveys in Kolkata, Nagpur, and Visakhapatnam. The method failed in the rest, where a non-Abbott (or change of testing assay) was likely used. We did not have sufficient data to reconstruct the sensitivity decay curve of Roche. Once it is available, a similar approach can be made readily. In Figs. 1 and 2, we assumed a peak sensitivity of 100% for Abbott, which could be too ideal (since the data collected were mainly symptomatic cases). For asymptomatic cases, the peak sensitivity could be as low as 80%. However, as long as the shape of the decay curve is kept, a factor (80%) on the whole decay curve can be translated into a factor in the IFR. The reciprocal of the IFR and the sensitivity decay rate appeared in a product form in our IAR and seroprevalence equation. Therefore, it would not change our final estimate of IAR and seroprevalence whether the factor is in IFR or in the decay rate.

Moreover, we formulated a simple method to reconstruct the IAR and estimate the seroprevalence of COVID-19 in India. Our simple approach works well in most of 12 Indian cities where serological survey data are available. We achieved this without knowing which cities used Abbott (except that we knew Abbott was used in Mumbai). In cities where our method did not yield a reasonable fit, a non-Abbott (e.g. Roche) or mixing of different testing assays were likely used. According to the available information, we observed that the serological testing equipment used in Mumbai is Abbott and Delhi used Mylab, German Altona Diagnostics, Roche, and ELISA. The devices used in Chennai include Abbott, Roche, and ELISA. The instruments used in Kolkata include Vitrros ECi, Ortho Clinical Diagnostics, Roche, and ELISA. The device Banglore used was the Elecsys Anti-SARS-CoV-2 assay. The equipment used in Ahmedabad was Zydus Diagnostics. The devices Pune used include ELISA and Roche. The device used in Surat was the ICMR National Institute of Virology. The devices Nagpur used include Roche and ELISA. The devices used in Coimbatore include Siemens and Abbott. The devices used in Jaipur include ICMR and IgM/IgG Duo Test Kit (SD, Biosensor, Republic of Korea). The device used in Visakhapatnam is unknown. An alternative explanation could be that the serological survey or death reporting is inconsistent in some cities where our approach fails. Our method provided a reasonable and reliable estimate of IAR by March 2021 in 12 Indian cities since it used both serological data and reported COVID-19 deaths.

4. Discussion

Sero-epidemiological studies are crucial in understanding the current and future scenario of the COVID-19 pandemic. Based on Backspace recent reports, the average seroprevalence of COVID-19 in India was medium, which indicates that a significant proportion of the overall population is still susceptible to COVID-19 infection (Murhekar, Bhatnagar, Selvaraju, et al., 2021). This further highlighted that the transmission could likely continue in most cities in India until the herd immunity threshold is reached. The herd immunity can be achieved either by previous exposure to the virus or through vaccination (Britton, Ball, & Trapman, 2020; Murhekar, Bhatnagar, Selvaraju, et al., 2021). However, the successful control depends on the individual susceptibility to infection, pre-existing immunity, and compliance of non-pharmaceutical interventions (NPIs) measures (Aguas et al., 2020; Lourenço, Pinotti, Thompson, & Gupta, 2020; Mendez-Brito, El Bcheraoui, & Pozo-Martin, 2021; Simoneaux & Shafer, 2020).

The IFR estimates in Table 1 are low. On the one hand, many serological studies found that a very large proportion of the population has been infected. On the other hand, the number of reported deaths is low (may or may not be due to under reporting). These two factors led to a seemingly low IFR in India. Banaji (Banaji, 2021) found a lower bound IFR in Mumbai at

0.1% with consideration of excess deaths (additional to reported COVID-19 deaths), which is not very far from our estimates here. Here we used reported COVID-19 deaths only, which could lead to a low IFR.

We estimated the seroprevalence rate, and reconstructed the IAR in 12 Indian cities. We showed that the seroprevalence rate was lower than the reconstructed IAR, which is a monotone-increasing function due to antibody waning. We aligned the reconstructed seroprevalence and serological survey to yield an IFR, which was applied to both the reconstructed seroprevalence and the IAR curve. These results are in line with previous estimates (George et al., 2021; Velumani et al., 2021).

A significant amount of people infected with SARS-CoV-2 do not show symptoms, yet they transmit the disease to other susceptible populations (Long et al., 2020; Oran & Eric, 2021; Tu, Tu, Gao, Shao, & Sheng, 2020). It has been reported that asymptomatic cases of COVID-19 could reach from 5% up to about 80% of all infections (Inbaraj, George, and Chandrasingh 2021; Yanes-Lane et al., 2020), especially for young and healthy individuals. In slums settings, these estimates could reach up to more than 90% (George et al., 2021; Velumani et al., 2021). Therefore, it is imperative to identify an infected individual at the early stage of the infection and trace all possible contacts in order to break the transmission of the virus, and Backspace to prevent large-scale outbreaks. However, recognizing an asymptomatically (and pre-symptomatic) infected individual is practically difficult (and sometimes impossible) since they might not seek medical attention (Gao et al., 2021; Inbaraj, George, and Chandrasingh 2021). As a result, relevant authorities did not recommend absolute reliance on the morbidity and mortality cases identified through RT-PCR (Inbaraj, George, and Chandrasingh 2021).

Furthermore, to tackle this issue, the concerned authorities suggested that more research should be done on sero-epidemiological surveys to generate more data that would help design the most effective control strategies ('World Health Organization. Coordinated global research roadmap: 2019 novel coronavirus; March 2020. Geneva: World Health Organization,' 2020). In addition, sero-epidemiological studies can help estimate the percentage of the population still susceptible to SARS-CoV-2. It is also important to investigate how antibody could provide immunity to the virus (Inbaraj, George, and Chandrasingh 2021). Most of early serosurveys, including the nationwide serosurvey across 21 Indian states by the Indian Council of Medical Research (ICMR), estimated the seroprevalence of COVID-19 in India to be 0.73% between May-June 2020 (Inbaraj, George, and Chandrasingh 2021; Murhekar et al., 2020). Subsequently (i.e., around August-September 2020), most serosurveys estimated the seroprevalence of SARS-CoV-2 in India to be 7–10% (George et al., 2021; Inbaraj, George, and Chandrasingh 2021; Khan et al., 2020; Murhekar, Bhatnagar, Selvaraju, et al., 2021; Murhekar, Bhatnagar, Thangaraj, et al., 2021). In their recent serosurvey study, Murhekar et al. estimated the overall seroprevalence of SARS-CoV-2 in India to be more than 24% (Murhekar, Bhatnagar, Thangaraj, et al., 2021).

The epidemiological implications of SARS-CoV-2 seroprevalence are that it helps identify whether herd immunity has been reached (due to vaccination or previous exposure to the virus). It also helps to identify more cases, especially asymptomatically infected individuals who do not usually show COVID-19 symptoms, to design the most effective control strategies to mitigate the epidemics. High estimation of seroprevalence would indicate that most of the population have been infected, and the herd immunity threshold will likely be reached (George et al., 2021; Kwok et al., 2021). Hence, the control efforts should be emphasized on recovering for the damages caused by this deadly virus, which includes suspension of control and intervention programmes, immunization and primary health care services for other infectious diseases; as well as rebuilding for better socio-economic development.

Our study has some limitations. We employed serological data that used multiple and mixing testing machines (Abbott and non-Abbott, e.g. Roche) to reconstruct an IAR and estimate the seroprevalence of COVID-19 in large cities in India. The true situation is much complicated than what we have considered. This could likely affect the estimation of seroprevalence in these cities. Further, we considered only 12 Indian cities; thus, interpretation for the overall situation has to be done with caution. We relied on the confidence in the COVID-19 death reporting.

5. Conclusion

We reconstructed the attack rate and estimated the seroprevalence in 12 large Indian cities. We argued that further seroepidemiological studies and improved COVID mortality reporting coupled with existing control strategies can effectively suppress the COVID-19 morbidity and mortality in India and beyond. Although we did not generate new data, we provided a way to connect data from different sources (COVID-19 deaths and serological survey). Hence, the overall confidence in results based on these data is enhanced and potential inconsistence can be revealed.

Ethics approval and consent to participate

This study only reanalyzed publicly available data which were carried out in accordance with relevant guidelines and regulations.

Consent for publication

Not applicable.

Availability of data and materials

Serological data used in this work were taken from the following references, Maine et al., 2021, Muecksch et al., 2021, Eberhardt et al., 2021, Kahre et al., 2021, Harris et al., 2021. Velumani et al., 2021. The COVID-19 deaths data for Indian cities were obtained from https://api.covid19india.org.

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Authors' contributions

All authors conceived the study, carried out the analysis, wrote the draft, revised the manuscript critically, and approved it for publishing.

Declaration of competing interest

The authors declare that they have no competing interests.

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None.

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