

Merits and Demerits of Selective Isolation of Superspreaders: A Mathematical Modeling Study Based upon West Bengal (India) SARS-COV 2 Data

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Abstract

Context: All COVID cases and their contacts are considered highly infectious requiring isolation, which blocks the COVID isolation beds and disrupts life in the community. **Aim:** To find out the effect of selective isolation and contact tracing of superspreaders as compared with the conventional ongoing protocol. **Settings and Design:** A mathematical model was designed to look at the effect of isolation and contact tracing of only those with high viral loads (superspreaders) on COVID-19 bed occupancy and overall mortality, in comparison with conventional protocol of isolation and contact tracing of all cases. **Materials and Methods:** An agent-based model, calibrated to the ongoing West Bengal COVID-19 data, was run for a total of 178 days to find out the effect of the interventions on COVID-19 bed occupancy and mortality. **Results:** There is an impressive reduction in the occupancy of COVID isolation beds, even with the preintervention testing rate with no negative impact on mortality. **Conclusions:** Strict isolation of superspreaders only, maybe highly effective in reducing the burden on health care and solving the COVID isolation bed crises if the testing rate is significantly increased.

Keywords: Coronavirus disease 2019, mathematical modeling, severe acute respiratory syndrome coronavirus 2, superspreader, viral load

INTRODUCTION

The first case and the first death were reported in West Bengal (India) on March 17, 2020 and March 23, 2020, respectively.^[1] The Government of India imposed lockdown on and from March 24, 2020 to May 31, 2020, with worldwide 20.9 million confirmed cases of SARS-Coronavirus 2 as on August 2020.^[2] During lockdown, only the local markets for daily consumption were open. It was, therefore, assumed that the source of transmission during this period was mainly the marketplaces, in a country like India where only 1.6% of the population has access to online shopping.^[3]

Technology based on RT-PCR allows for the calculation of viral load in terms of cycle threshold values (ct values), which is normally not reported. Until now, there are few published reports, with viral loads of SARS-COV-2 in relation to severity of the disease but have only yielded conflicting results.^[4-6] However, there is less doubt about the relationship of transmissibility of the disease with viral loads.^[7]

National Institute of Occupational Health, Ahmedabad, India, conducted a study with 138 SARS-CoV-2 positive samples out of a total of around two thousand samples collected in a district of Gujarat, India in April and May 2020, and follow up with the secondary cases. Only 7% of the SARS-COV-2-positive samples demonstrated high viral load, demonstrating these people, would on average, transmit the infection to 6.25 other people, whereas the vast majority (84%) had a low viral load, transmitting to only 0.8 person on average. Nine percent had a moderate viral load. This observation has led the investigators to propose more studies to look at the effect of isolation of these superspreaders (high and moderate viral loads) selectively on

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the transmission in the community.^[8] Based on this study, this mathematical model has assumed a similar effect of viral load on transmission dynamics; other assumptions include higher mortality among elderly subjects, population density in the market places being high enough to represent the population density of the aforementioned study.

The model has utilized the West Bengal COVID data^[9] from March 14, 2020 to June 23, 2020, for its calibration.

MATERIALS AND METHODS

The fundamental principle of this agent-based model is the (as yet) known virus-host interaction, with subsequent clinical consequences, which terminates with either recovery or mortality.

Once the model gains acceptance with real world data, the second part begins with interventions and future prediction. On the 23rd day of unlocking, for 178 days since the date of intervention, the model has attempted interventions in four groups:

1. Current strategy with the same rate of testing as that of West Bengal government real word data on June 23, 2020
2. Current strategy with four times the rate of testing as that of West Bengal government real word data on June 23, 2020
3. Reporting of viral load (ct values) routinely to all positive cases, with the same rate of testing as that of West Bengal government real word data on June 23, 2020
4. Reporting of viral load (ct values) routinely to all positive cases, with four times the rate of testing as that of West Bengal government real word data on June 23, 2020.

It is to be noted that in the 3rd and 4th groups, only the high and moderate viral loads have received special attention, whereas low viral load cases have received standard attention, as per the government protocol.

The primary endpoints are as follows:

1. COVID bed occupancy
2. Mortality.

Several assumptions have been made on the basis of observational data:

1. Markets are the main source of spread of infection.
2. A person with low viral load will infect 0.8 persons when going to market. Among the superspreaders, that is, persons with moderate and high viral load will infect 3 and 7 persons respectively when going to market^[8]
3. The viral load distribution in the population is same in all age groups, 84% constituting low viral loads, 9% moderate viral loads, and 7% high viral loads^[8]
4. Percentage of low viral load in hospitalized participants is 61%, whereas moderate/high viral load makes up 39% of the hospitalized participants^[7]
5. Asymptomatic COVID cases have been considered with the assumption that 30% of infections will not produce symptoms

6. In case of ct intervention (3rd and 4th group), people with high/moderate viral loads have 1/3rd of their contacts randomly traced and tested
7. In case of current strategy of testing, isolation and contact tracing, 1/3rd of contacts of the individual are randomly tested regardless of viral load
8. Family structure consists of four members per family
9. One person from each family is designated to go to the markets, which means 25% of the total population goes to the markets. This market going population consists of elderly (>60 years) and younger adults (<60 years)
10. The elderly (>60 years) comprises 7.4% of the West Bengal population^[10]
11. 2.96% of the total market going population comprises of elderly people
12. Probability of death was assumed to be independent of viral load
13. Mortality rate figures have been taken from West Bengal Government data on mortality.^[9]

Sensitivity analysis has been done using MATLAB 2020a software (Manufacturer: MathWorks, City: Natick, Massachusetts, USA).

RESULTS

Here, the model has tested its validity with the ongoing regularly published West Bengal COVID data,^[9] with real world data of numbers and location of markets across the state with areas showing different levels of transmission designated as Red (High), Orange (low), and Green (no transmission). Graphs [Figures 1 and 2] comparing real world data and simulation data on daily COVID positivity and number of deaths have shown excellent congruence in terms of trend on timescale and also numerically, except a few unexplained discordance which is natural in the real world with too many unknown and transient variables which

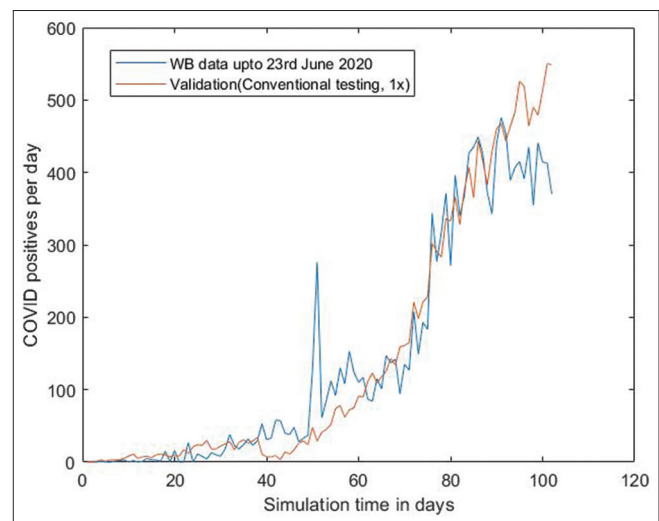


Figure 1: COVID positivity per day: The trajectory of the two curves is nearly congruent (calibration of model to real word data)

include both human and nonhuman factors. Incongruence in mortality [Figure 2], however, is believed to be due to the following reasons:

- For a period of time in West Bengal, mortality statistics did not include COVID positives whose deaths could possibly be contributed by comorbidities
- Most recorded deaths are hospital deaths and it is likely that many deaths in the community, particularly those with multiple comorbidities happened before any opportunity for testing. The Model, on the other hand, will pick up all COVID positive deaths in both hospitals and community.

Routine viral load testing and selective isolation of superspreaders, with the same rate of testing as on June 23, 2020 have shown increase in the number of superspreaders and this maybe because of large percentage of low viral load subjects, who have not been isolated. This large population of low viral load should induce significant numbers of superspreaders, in spite of their low infectivity, but the number drops, despite high level of detection to a level comparable with conventional strategy if testing rate is quadrupled and the reason is intensive contact tracing and strict isolation of superspreaders with highest level of vigilance. Similar effect has been observed with mortality [Figures 3 and 4].

Viral load testing strategy improves COVID isolation bed availability significantly with immediate effect. On the contrary, in conventional testing strategy, it rather worsens initially with increased testing rate, followed, by a fall in bed occupancy, but still remains higher on time scale [Figure 5].

DISCUSSION

The concept of superspreading events is a known entity and has been associated with many other infectious diseases such as typhoid, tuberculosis, measles, Ebola hemorrhagic fever, HIV, and SARS.^[11-18]

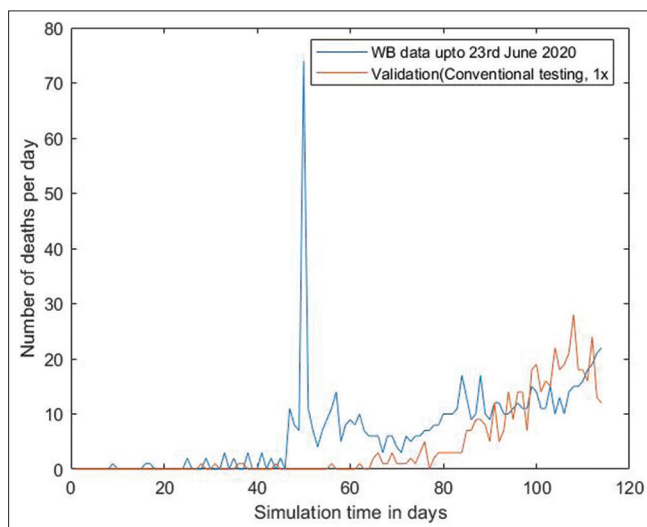


Figure 2: Death: Simulation for over 100 days since the onset of lockdown has calculated daily number of deaths which, however, fails to match closely with number of reported deaths (calibration of model to real word data)

Predicting and identifying superspreaders, therefore, offer distinct advantages in the management and preparedness of this COVID-19 pandemic. The problem lies in the paucity of adequate clinical data. Published literature on this issue reported conflicting data so far and could not establish any consistency in the relationship of viral load and severity of the disease.^[4-6]

However, about transmissibility of the disease, especially in the community, opinions are more or less concurrent,^[8,19] although some strong opinion has been raised about heterogeneity in the standardization of testing method and human errors associated with collection and transportation of samples.^[20] However, this model has assumed perfection in the quality and reporting of the testing.

As opposed to the result of our model, increasing testing rate fourfold could not contain the disease in reality, because of impracticability of tracing all the positive cases and also increasing noncompliance post lockdown. However, isolating and contact tracing only 16% of the total positive cases, that is the superspreaders is not an impractical proposition, even in a resource deprived country, and this model has demonstrated an impressive containment with this strategy, if the testing rate is increased fourfold, which is in fact the current situation, without any negative impact on mortality.

At the peak of the disease load in the community, there is a very high demand for hospitalization. Unless there is a steady flow of transfer to nonisolation zone, isolation zones get quickly filled up and remain blocked with a large number of low viral load patients who could otherwise be shifted to nonisolation areas, creating vacancy in the isolation areas for treatment. This model has predictably proven that point, at all levels of

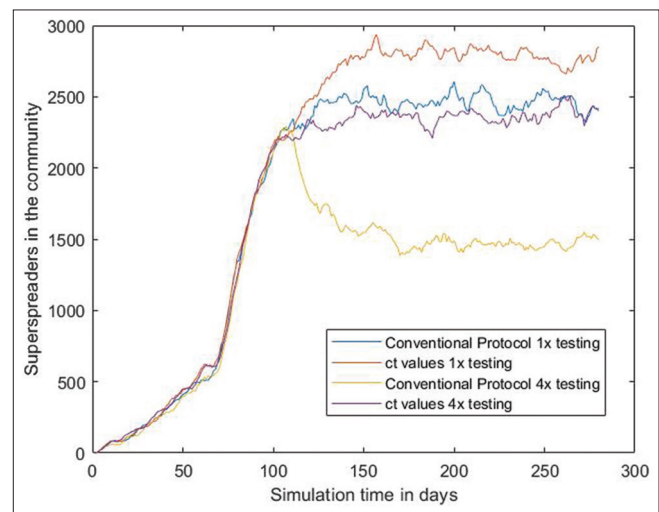


Figure 3: Superspreaders: Routine viral load testing and isolation of only superspreaders shows significant increase in total number of superspreaders. If the testing rate is quadrupled, the numbers converge to the conventional protocol with preintervention testing rate. In conventional protocol, however, increased testing ($\times 4$) results in decline in the number of superspreaders

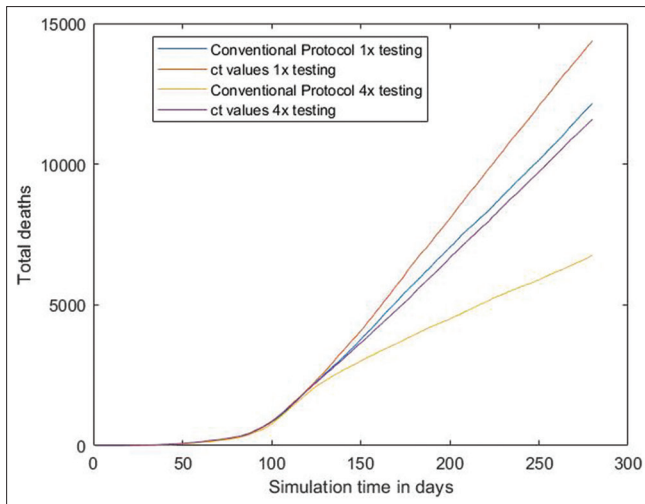


Figure 4: Deaths: Routine viral load testing and isolation of only superspreaders shows significant increase in total mortality. If the testing rate is quadrupled, the numbers roughly converge to just below numbers of the conventional protocol with preintervention testing rate. However, with increased testing ($\times 4$), conventional protocol shows reduction in mortality

testing rate. This is an exciting proposition, and a multicentric clinical study to prove the efficacy and safety of this strategy is important and a need of the hour.

Weakness of this modeling study is too many assumptions which are based on relatively weak evidences.

The strength of the study is that the assumptions are reasonably logical and have addressed practical issues which are critically important in the containment of a pandemic in a country with high population density, and it is validated with real world data, thus justifying correctness of the assumptions. The closest real life evidence of this model is a pilot study conducted and published by one of the authors in Ahmedabad district, where institutionalized quarantine of high viral load subjects resulted in demonstrably faster decline in active cases than rest of Gujarat.^[21]

CONCLUSIONS

This mathematical modelling study concludes that isolating and paying special attention to only superspreaders selectively is an effective strategy in a resource-deprived overpopulated nation, provided the overall testing rate is considerably increased, particularly at the peak of transmission, when COVID isolation bed crisis is unmanageable. This justifies the merit of the strategy. However, safety of this strategy needs to be ensured by minimizing heterogeneity and subjectivity in the entire process of testing methodology, requiring more vigilance, and raising the urgent need for more clinical, population as well as biotechnology-based research. This is the shortcomings or demerits of viral load testing strategy at the current level of understanding.

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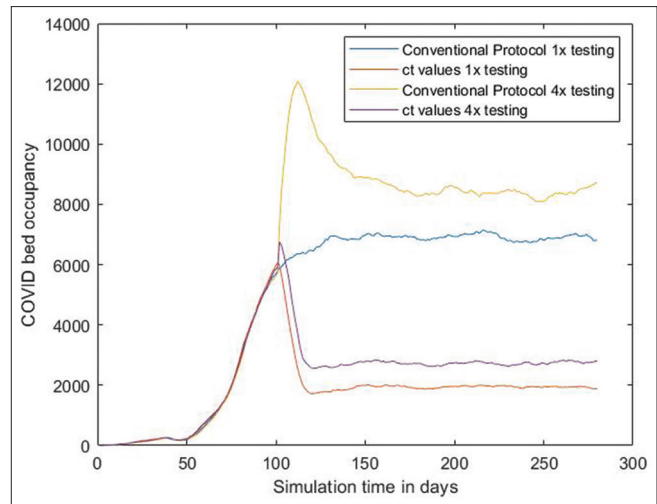


Figure 5: COVID bed occupancy: Routine viral load testing and isolation of only superspreaders shows remarkable decline in COVID bed occupancy, both in preintervention and increased testing levels. However, conventional protocol, with increased testing, results in an increase in COVID bed occupancy and remains so over time

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Conflicts of interest

There are no conflicts of interest.

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