Models and Supermodels; Foreseeing the Future of COVID-19 Pandemic-A Narrative Review

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ABSTRACT

Currently, the world is under a threat from COVID-19 which is a new disease spread by a virus of Corona family. Majority of countries of world have noticed a huge number of COVID-19 cases from December 2019 onwards. People with low immunity, old age, and associated co morbidities have severe COVID-19 infection with increase mortality. The symptoms of COVID-19 are cough, cold, breathing problem very similar to flu. It is observed by the doctors that a person infected by COVID-19 is recovered within 14-16 days because the incubation period of novel Corona virus is of fourteen days. COVID-19 is now a pandemic as declared by World Health Organization (WHO).

If hospitals are not well prepared, then it is not possible for health workers to operate efficiently. In this situation it is inevitable to have an accurate estimation of new COVID-19 cases, which can help the medical and administrative authorities. Further, it is also very important too know that which country is facing how much severity of this disease. It is reported that there are three important stages of COVID-19; stage-II and stage-III. In stage-II, there is person to person transmission and in stage-III, there is a community transmission. According to the stage of COVID-19, plan of action by different countries can be decided.

In India, the first case of COVID-19 was reported on 30 January 2020, originating from China. After two months this disease spread in almost all parts of the country. After the first wave, the second wave of COVID-19 pandemic created havoc. The world is probably waiting for the third wave. But; how is the third wave going to hit is debatable. With on-going mass vaccinations on one hand to evolution of new mutants at the other, the scientific dilemma continues to haunt. Mathematical models/supermodels were created to predict natural course of disease by think tanks all over the globe. This narrative review focuses on these mathematical models and their utility in prediction of the COVID-19 pandemic.

Key words: Mortality, Models, Transmission, Stage, Community

INTRODUCTION

Humankind has been aware of outbreaks of infectious diseases encompassing entire nations or civilizations since antiquity like pharaonic plagues in Ancient Egypt (1715 BC) [1], the 'cocoliztli' epidemics in Mesoamerican native population during 16th century, bubonic plague in Europe (1348) [2], pandemic influenza (1918–1919) affecting America, Europe, Asia, and Africa, less severe influenza pandemics in 1957 and 1963, Human Immuno-deficiency virus (HIV) (1981), Severe Acute Respiratory Syndrome (SARS) (2003), pandemic H_1N_1 (2009), Middle East Respiratory Syndrome (MERS) (2012), avian influenza (H_7N_9), and Ebola (2014–2016) [3].

Because scientists and researchers desired to understand the dynamics and progression of a novel epidemic/pandemic in the population, they developed numerous methodologies and approaches of mathematical modelling with diverse assumptions and approaches. The initial mathematical model credit goes to Bernoulli, et al. who analyzed the mortality due to smallpox in England and showed that inoculation against the virus would increase the life expectancy at birth by approximately three years [4]. Later, the foundations of mathematical modeling for infectious diseases were established by Kermack, et al. [5]. The early models defined people as Susceptible, Infected (infectious) and Recovered (SIR) and it is a typical model for any pandemic dynamics that divides the population into three categories: Susceptible (S), Infected (I) and Recovered (R). Recovered has a subcategory called Deceased (D). To distinguish between asymptomatic and symptomatic individuals, a new category is introduced:

SIR model category I is split into A (asymptomatic patients) and I (symptomatic patients). When infected, a person's immune level, genetic disposition, comorbidities and other physiology determine whether he or she falls into category A or category I. This divides S into two categories: SA (which transitions to A following infection) and SI (these transition to I upon infection). Further advancements result in increasingly sophisticated compartmental models, such as age structure and so on [6]. With each successive epidemic/pandemic, more techniques and technologies, including machine learning, are being employed for mathematical modelling. There are three types of infectious disease models based on statistical, mathematical/mechanistic state space and empirical/machine learning [7].

LITERATURE REVIEW

Models and COVID-19 pandemic

SARS-CoV-2 first appeared on the horizon in late December 2019, when a number of Chinese local health officials reported clusters of patients with pneumonia of unknown origin. The pathogen (SARS-CoV-2) was identified. As of April 24, 2020, the SARS-CoV-2 virus has spread to 210 nations, with 2,697,316 cases and 188,857 mortality [8,9].

Extrapolating from the present and applying what we've learned from the past to predict the future is becoming increasingly essential. It's crucial to know how many individuals are now sick so that we can predict how many cases of COVID-19 will be observed in the future. To do so, we'll need to know the disease's historical trajectory as well as how infected people transmit the virus. So the Indian government top agency department of science and technology hence supported the development of single supermodel for COVID-19 in India which combines best features of model from India and worldwide to predict the nature, the spread of the virus, the second wave of the disease in the country to help make short and long-term plans to fight against the deadly disease. A high level committee composed of eminent scientist including several epidermiologist was set. The report of committee is in form of the "national supermodel committee" and it is now available on Indian journal of medical research.

The report is divided into two sections. The first section contains broad suggestions for India. They have more weight because of the panel's prominence. It cautions that advances made in recent months will be rendered meaningless if distancing measures are decreased during the forthcoming festival season, emphasises the need of continuing to pay attention to masking and advises that if we pay attention to these conditions, there may hope to enter the new year without seeing any further sustained increase in the number of cases. All these points are almost certainly valid and report was signed by all the members of committee. The second part in the published paper is about the supermodel. Only 3 members of this committee are the author of this paper. The authors are eminent computer scientist, mathematician famous for work in control theory and ex-army officer with a medical background. All are well known names. None are epidemiologists even though the committee as a whole possessed this expertise.

The supermodel assumes something unusual. All generally accepted models for COVID-19 so far assume that everyone is equally susceptible to it. Nothing we know suggests that this should not be the case. But, an unusual feature of COVID-19 is that some fraction of people infected with the virus does not display symptoms, while being able to infect others. About 30-60% of those infected, perhaps more, are such asymptomatic carriers of infection. The large presence of such asymptomatic patients, who do infect others they come in contact with, changes the dynamics of disease. Instead of the total infected population, number of seriously impacted persons, which is significantly less, becomes more important since only they require major medical intervention. Why this is so is still unknown. Thus estimates for medical inventory, including oxygen, ventilators, ICUs beds etc. needs to be made based on projections of this number. At the same time, asymptomatic patients need to be advised isolation so they do not spread the infection.

Supermodel takes a new route to explain this that virtually no other model takes. It assumes that the population prior to infection can be divided into two separate parts. One part will always be either asymptomatically infected while the other with symptoms. The supermodel assumes that "immunity levels, genetic disposition and co-morbidities" might determine this assignment. We can take example from random sub-set of people, say healthcare workers drawn from the general population, we should then expect to see the same proportion of asymptomatic versus symptomatic patients in them as in the general population. This is not what is seen. Around the world, healthcare workers are at more risk of severe infection and death than members of the general population. This suggests that it is the amount of exposure to the virus that may be important in determining whether an individual will exhibit symptoms.

A model should have as few numbers as possible that must be provided by the modeler to describe the data (they're called parameters). For virtually all such models, such parameters must be estimated. The more the number of parameters, the larger the significance of uncertainties in these numbers, even as more parameters provides more flexibility. The supermodel ostensibly has just four parameters. It fits the count of new cases well, reproducing the recent peak in Indian cases as well as the two peaks that Delhi saw. The model divides the period between the start of the pandemic and the date at which the results were obtained into six parts. These four parameters all take different values in each of these parts. This gives 24 parameters in all, all separately varied to fit the case count. These parameters are not constrained in any way by an understanding of COVID-19 epidemiology. Worse, some of the parameters are then

varied across a large range, from 67 to 4,75,000 in one case. There is no justification provided for this. It makes little sense to have so many parameters, all changing, in a model. Indeed, a famous quote from the mathematician John von Neumann applies here: "With four parameters I can fit an elephant and with five I can make him wiggle his trunk".

DISCUSSION

In India over 4,00,000 cases are being registered every day In India amid the second wave of the COVID-19 pandemic, and thousands of people succumb to the deadly virus in less than a month [10]. The numbers have left everyone from the public to government officials in concern. There have been discussions earlier about whether India will face the second wave or not. Still, now as we are here tackling the deadly pandemic, several scientists and experts blame the Sutra model for creating a perception that India is most likely not to face the second wave. SUTRA stands for Susceptible, Undetected, Tested (positive) and Removed Approach, a government-backed model or prototype. Most of the scientists from IIT Kanpur and Hyderabad have applied this Sutra concept to predict the trajectory of COVID-19 in India. This model came into the public eye when one of its members declared in October last year that India is past its peak of the pandemic and announced that it is most unlikely for us to be hit by a second wave. Now, they are being slammed as both of their significant prophecies proved to be utterly wrong as the on-going second wave, raising cases and deaths are definitive proof of the contrary.

Parameters used in this model are beta, also known as contact rate, measures how many people are infected by an infected person per day. Reach is a measure of the percentage of the population exposed to the pandemic. Epsilon is the simple ratio of cases that are detected to undetected cases of the virus. This model helped in dividing the patient population into symptomatic and asymptomatic cases. With the help of contact tracing, some fraction of asymptomatic patients could be detected, but there were also large numbers of undetected patients who had no symptoms of the virus. It is believed that the spread of a pandemic over time is through a parameter called 'reach'. Numerically stable methods are used to estimate the parameters in our model and ratio of infected to uninfected detected. This model has been used to predict the progression of the COVID-19 pandemic in several countries. The data on the number of recovered patients is available, Scientists predict the number of active cases as a function of time. This resulted in the conclusion that India had a smooth rise followed by an equally smooth fall-off in the number of active cases. For other countries too, the predictions closely matched the observed outcomes. Another important contribution of mathematical models is the qualitative information generated by each model, which provides a range of inputs to the planners at various levels.

There is a lot of difference in the numbers between the models, which might be due to the models' varied assumptions and the mathematical models' predictions for different time periods. As a consequence, it was unable to synthesise the pooled result. The study discovered a reasonable correlation for short-term forecasts, stressing the necessity for predictive model adjustments as more and more data becomes available. Long-term forecasts may be problematic due to the fact that predictive models are built on sparse inputs for the sake of greater understanding, and assumptions may not accurately mimic real life circumstances. These short-term forecasts, on the other hand, are critical for health planners, decision-makers and others to allocate appropriate resources to combat epidemics. Particularly in a developing epidemic like COVD-19, complex or hybrid models with explicit assumptions covering essential ones such as the influence of non-pharmacological treatments, age structure, interactions, stochasticity, quarantine, isolation, socioeconomics and so on are necessary. The majority of the models did not account for unclear data, which is a key paradigm in epidemiology. This, however, may be ascribed to a lack of data to begin with, rather than a criticism of the strategy or methodology used.

There are several issues with super models, such as variability like there have been several cases where Sutra projections have been shown to be beyond the boundaries of the actual scenario, and predictions that are made are too variable to be used to influence government action. Sutra model uses too many parameters hence was difficult to compute since it relied on so many factors, and all of them had to be re-calibrated every time it was used. The more parameters you have, the more you are in danger of predicting the future reliability. The Sutra model omits the importance of the behaviour of the virus. For example, some people were more significant transmitters of the virus than others. The value of the 'beta' parameters in the Sutra model increases as new variations appear every few months. Changes in parameter values are also observed by the model. It is unconcerned with or exaggerates the explanation for the shift. Because the virus altered its route frequently and in a short period of time, the predictions needed to be updated as well, but this did not happen. Its validity was further harmed by its failure to account for social or geographic circumstances, as well as connections between different age groups.

Scientists and specialists working on the Sutra model for Corona said that they projected that about 1 lakh instances would be reported in the third week of April; however their assumptions were incorrect since they were using a mathematical model. They claim that they can function this way and be accurate only if the virus's dynamics and nature do not shift over time. But in India's case, the virus has constantly been changing and they have to make changes almost every day. Though they could not predict the exact nature of the second wave, they continue to work on the future course and help in finding accurate projections.

As a result, the fast availability of models, many of which are not peer-reviewed, as well as the availability of models to the lay press and their own interpretation, is fraught with the risk of models falling out of favour. As academics and planners, we must look beyond the simple answers provided by models (magnitude, numbers and fatality) and instead utilise models to try to put policies which may change the predictions by various scenarios for the greater public good. Models should also be understood in the context of the overall system, taking into account other medical problems, as well as social, economic, cultural, and ethical issues. It should be considered as one of several planning inputs. There is minimal room for subjectivity in mathematical modelling because it includes equations and predictions are made by solving them. Another important limitation is to check for the quality of studies of the mathematical modeling. Now with more data availability, the future models for India may also look at further refinements using different approaches and tools for better use of quantitative outputs of the models [11,12].

There are a slew of other issues with the model and the results it generates. However, simply this conversation should demonstrate that the government's policy is unfit to deal with the proliferation of COVID-19 in India. It's risky to base public health policy on faulty models, because people's lives are on the line, and false optimism comes with consequences. Science should not serve political ends. There are better models. Choosing this one to be India's 'supermodel' presents a misleading picture of India's capabilities in both epidemiology and modelling, to Indians as well as to the rest of the world. A preliminary examination of these models for India found significant differences in scope, assumptions, numerical predictions, the path of the pandemic in India, the impact of various actions, the impact on health care systems, and so on.

CONCLUSION

Knowledge of model drawbacks is important for ensuring useful information to policy makers as well as to the general population. More efforts should be exerted if mathematical models are used to know the impact of core assumptions on the consequences, outcomes or estimations and also in analysing the model's sensitivity to various parameter values of various ranges. When a major disease outbreak or health crisis of communicable diseases occurs, there is little time to develop models or approximate criteria. As a result, having backup plans based on various circumstances and modelling techniques is critical for successfully overcoming a health emergency. So, it is better to follow all the preventive measures for COVID-19 by washing hands frequently, avoiding touching the mouth, nose, and face, avoiding going in crowded place and by maintaining social distancing (1 meter or 3 feet) with other people. It is noticed that lock-down and isolation are the important techniques to prevent the spreading of the disease. If people detected positive for COVID-19 they should be home isolated or quarantined in a hospital or any quarantine centres. Various undetected cases in community should be masked properly when they make contact without normal population to prevent spread of infection. Many drugs and attempts have been tested, including drugs used before for management of viruses particularly SARS and HCV as well as convalescent plasma, but there is no consensus regarding the management and control of the current epidemic up till now. Until achievement of such progress, universal precautions for avoiding infections transmissions should be taken into consideration. These drugs included use of ribavirin, glucocorticoids which is only used as per WHO when COVID-19 is associated with exacerbating obstructive airways. Lopinavir and ritonavir which are protease inhibitors used in 2003 SARS cases. Remdesivir (GS-5734) preclinical study showed great significance against Coronaviruses. Historically, the large proportion of approved vaccines were focused on inducing strong protective neutralising antibodies against the target pathogen, with the goal of granting sterilising immunity in vaccinated individuals. Attenuated live pathogen vaccine methods employ delivering a weakened form of the live pathogen. Subunit vaccines are made by either purifying antigen from pathogens cloned in cell culture systems. Inactivated pathogen vaccines contain entire pathogens that have been inactivated chemical treatment or heat. Viral vector vaccines are built on a genetically modified adenoviral or measles platform. Finally, while nucleic acid (DNA and mRNA) vaccines are easy to make, they have yet to be tested as effective human vaccine techniques. On January 16, 2021, free immunisation against COVID-19 began in India, and the government is trying to encourage all people to be immunised as a part of world's largest vaccination programme. Four out of the eight vaccines were developed by India itself. COVISHIELD (Oxford-AstraZeneca vaccine) and COVAXIN (a home-grown vaccine by Bharat Biotech) have been approved for limited emergency use by India's drug regulation government body. Indian manufacturers had already confirmed that they will be able to meet the country's long-term COVID-19 vaccine needs.

The interpretation and readily accessible results show that there has been no community spread in India so far, *i.e.*, the majority of the population are not exposed to virus or infected or spreading the disease and infecting other people due to lock-down and quarantine.

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