Editorial

Is Everything Okay? COVID-19

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It is very painful and tragic to seek and hark "is everything okay?" We are facing an unprecedented medical, social, and economic crisis from the dreadful pandemic of novel corona virus disease 2019 (COVID-19) since it has emerged from Wuhan, China.

As of March 28, 2020, a total of 512,701 confirmed cases and 23,495 deaths[1] had taken place with no respite in geographical spread, mortality, morbidity, and economic loss due to the outbreak of COVID-19. World Health Organization (WHO) had declared this outbreak as a public health emergency of international concerns on January 30, 2020. Subsequently, all the countries had took perception of situation to their prime concern after an initial slack and unreadiness at the cost of their lives and livelihood. Together, all have started the campaign vigorously to "fight, unite, and ignite a global movement for eradicating this "virus outbreak."

"Is everything okay? This question repeats over and over again in our minds and thoughts to introspect in many ways. On March 13, WHO said that Europe was now the center of the pandemic. A few days later, deaths in Italy[2] surpassed those in China to reach 10,000 as of now. Iran and Spain had also reported over 1,000 deaths as of March 23. With the second highest populated country, India had a total of 27,688 samples from 26,798 individuals tested for SARS (severe acute respiratory syndrome)-CoV2 as on March 27, 2020, where 691 individuals have been confirmed positive among suspected cases and contacts of known positive cases with <2% death.[3] On March 25, it announced a remarkable country-wide shut down for 21 days to cut the transmission chain of the novel coronavirus SARS-CoV-2.[4] Many others like the United States, United Kingdom, Australia, Europe, as well as Middle East countries, dynamically initiated the containment measures of screening, testing, and tracing contacts.

The United States which has 103,321 cases with 1,668 deaths is heralding an imminent wave of fatalities.[5] Centre for Disease Control and Prevention (CDC) has released a statement on self-quarantine guidance for greater New York City transportation and delivery workers[6] and COVID-19 apple application[7] to guide Americans through a series of questions about their health and exposure to determine if they should seek care for COVID-19 symptoms. The tool provides CDC recommendations on next steps including guidance on social distancing and self-isolating, how to closely monitor symptoms, recommendations on testing, and when to contact a medical provider. In addition, they greatly emphasize that people take precautions to stay safe and keep others safe, including washing their hands regularly, staying home when sick, covering coughs and sneezes, and maintaining distance from others and self-quarantine for 14 days who were recently in the affected areas of New York.

For the first time, WHO is asking the general public and private donors for their support. The project is a test run for the WHO Foundation, to be launched later this year. The COVID-19 Solidarity Response Fund for WHO, managed by the United Nation Foundation and the Swiss Philanthropy Foundation, has been launched to raise money from individuals, the private sector, and foundations to finance WHO's response to the coronavirus disease 2019 (COVID-19) pandemic. It was launched on March 13, and 10 days after its launch, it had raised $71 million from 170,000 individuals and organizations, including Facebook, Google, and FIFA which will not be suffice considering the future medical requirements and needs. It could soon fall short or run out of funds. The best health care facilitated countries are struggling to acquire diagnostic tests, personal protective equipment, and ventilators for overwhelmed hospitals with new and affected COVID-19 caseloads. According to WHO, almost 30% of countries have no COVID-19 national preparedness and response plans, and only half of countries have a national infection prevention and control program and water, sanitation, and hygiene standards in all health care facilities.

Despondence, indecisiveness, angry, pain, grief, uncertainty, helpless, mistrust, and no confidence prevail everywhere in the world. The governments, bureaucrats, health care, and

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paramedical workers are tireless working and struggling with the fragile health care facilities to deliver the best possible treatment despite challenges and dangerous conditions. With no basic facilities, like gloves and masks, inadequate supply of personal protection equipments, and overloaded cases in the isolation wards, ICUs, their incredible commitments to their communities at this viral outbreak is something akin to GOD. Despite the bad time and bleak conditions, images of solidarity have emerged. Many neighboring countries, entrepreneur, business men, medical associations, nongovernment organizations (NGOs), Rotarians, and other kind-hearted voluntary support groups have graciously stepped up to provide support in all possible ways.

Indian Medical Associations (branches) understood the growing importance of social and collective commitments to the community, have volunteered with the Indian government to tackle the critical care cases, supply of personal protective equipments (PPEs), ventilators, N95 masks, and allotment of beds in private nursing homes for COVID-19 cases in addition to 24 × 7 helpline. Globally, every possible events and shows have been put off in the hope of effective containment.

Let's quickly analyze the early dynamics of transmission and control of COVID-19 with the published mathematics model study and from Wuhan model inference. A key parameter is the basic reproduction number (R_0), which determines how fast SARS-CoV-2 can spread through the population during the early stages of the outbreak. This is an inherently difficult parameter to estimate, since the true number of cases that can transmit infection at a given time is unknown (reported cases are likely to be just a small fraction of true cases) and probably varies over time (because of different interventions being introduced and population behavior changing in response to the epidemic).[8] However, there are several challenges to such analyses, particularly in real time. There can be a delay to symptom appearance resulting from the incubation period and delay to confirmation of cases resulting from detection and testing capacity.

To examine the potential for new outbreaks to establish in locations outside Wuhan, estimates of the R_t is used to simulate new outbreaks with potential individual-level variation in transmission (i.e., so called superspreading events). Presumably, if transmission is more homogeneous, with all infectious individuals generating a similar number of secondary cases, it is more likely than an outbreak will establish. Based on the median R_t estimated during January before travel restrictions were introduced, estimation of single introduction of SARS-CoV-2 with SARS-like or Middle East respiratory syndrome (MERS)-like individual-level variation in transmission would have a 17 to 25% probability of causing a large outbreak. Assuming SARS-like variation and Wuhan-like transmission, every four or more infections have been introduced into a new location, there is an over 50% chance that an outbreak will occur.[9] Such is the fatal viral transmission in the community.

WHO director General at his press brief on March 25, 2020 said "shutting down population movement is buying time and reducing the pressure on health systems. But on their own, these measures will not extinguish the epidemic. The point of these actions is to enable the more precise and targeted measures that are needed to stop transmission and save lives." Among the six steps that every country should take, as the WHO chief said, the production, capacity, and availability of testing should be ramped up and a system to "find every suspected case at community level" must be implemented. The six measures are the "best way to suppress and stop transmission, so that when restrictions are lifted, the virus doesn't resurge," he added.[4]

India's lockdown for 21 days would be a great social experiment which allows social distancing. If followed strictly, it will contribute to delayed peak and to an extent, in flattening of the curve. Lockdowns may have to get extended in the areas with high transmission. It is important to identify such areas. Although started late, the Wuhan shutdown slowed the dispersal of infection to other cities by an estimated 2.91 days, delaying epidemic growth elsewhere in China. Other cities that implemented control measures preemptively reported 33.3% fewer cases in the first week of their outbreaks compared with cities that started control later. The most effective interventions were suspending intracity public transport, closing entertainment venues, and banning public gatherings. Combining a mathematical model with multiple datasets, median daily R_t of SARS-CoV-2 in Wuhan probably varied between 1·6 and 2·6 in January 2020, before travel restrictions were introduced. The transmission was declined by around half in the 2 weeks spanning the introduction of restrictions.[9] Given clear values and data, the dynamics of how the disease spreads from person to person are still uncertain and unclear. It is too early to provide conclusive evidence regarding this. Like SARS, emerging evidence shows that SARS-CoV-2 RNA can be detected in stool samples. A study has found extended duration of viral shedding can occur in faces for nearly 5 weeks after respiratory samples turn negative for SARS-CoV-2.

Apart from mathematics, let us see the time frame (median) and its implications in the COVID-19 outbreak mitigation which I hope to provide valuable inputs to society, health care workers, policy makers, and the rest of the world.

- Basic reproduction number, R0: 2·2 (1·6–3·0) days.
- Average incubation period: 6·4 days.
- Average duration of infection: 3 or 7 days.
- Initial number of infected: 200 or 2,000.
- Probability of infection acquired from subclinical: 0.25.
- Probability of infected case is clinical: 0 or 0·4–0.8.

The lockdown is an opportunity for us to mitigate the basic reproduction number, contain individuals in their incubation period, and prevent spread of infection. The probability of infection event can be reduced by rapidly scaling up the capacity to have enough resources to manage, isolate, and provide intensive care for those who needed it. Both measures going hand-in-hand capacity could have a reasonable effect on flattening the epidemic curve. Given the inadequate testing facilities in both governments and private health care providers, especially in low-income

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countries and countries without insurance back up, a syndromic approach to manage every case of fever, cough, and respiratory distress as COVID-19, unless otherwise proved, will make things better.

If given adequate testing facilities, the best strategy is to test among the SARI (severely affected respiratory infections) admitted in the hospitals and the OPDs (outpatient departments) along with strong national and local surveillance to prevent eruption of illness suddenly in large numbers of people (resurgence).

Sustained physical distancing have a strong potential to reduce the magnitude of the epidemic peak of COVID-19 and lead to a smaller number of overall cases. Lowering and flattening of the epidemic peak is particswth care system. Premature and sudden lifting of interventions could lead to an earlier secondary peak, which could be flattened by relaxing the interventions gradually.

Chloroquine, by increasing the endosomal pH required for virus-cell fusion, has the potential of blocking viral infection and was shown to affect activation of p38 mitogen-activated protein kinase (MAPK), which is involved in replication of HCoV-229E. A combination of the antiretroviral drugs lopinavir and ritonavir significantly improved the clinical condition of SARS-CoV patients and might be an option in COVID-19 infections. Further possibilities include leronlimab, a humanized monoclonal antibody (CCR5 antagonist), and galidesivir, a nucleoside RNA polymerase inhibitor, both of which have shown survival benefits in several deadly virus infections and are being considered as potential treatment candidates. Clinical trials presently registered at ClinicalTrials.gov focus on the efficacy of remdesivir, immunoglobulins, arbidol hydrochloride combined with interferon atomization, ASC09F + oseltamivir, ritonavir + oseltamivir, lopinavir + ritonavir, mesenchymal stem cell treatment, darunavir + cobicistat, hydroxychloroquine, methylprednisolone, and washed microbiota transplantation.[10]

Of the late, Codagenix Inc., a U.S. firm, and Serum Institute of India, have entered into a partnership, to rapidly codevelop a vaccine for COVID-19.

It is imperative that the global community takes advantage of all possible lessons learnt from Wuhan and other countries; available medical expertise along with global spirit of cooperation under the leadership of WHO to combat this evil suffering prudent and diligently. WHO is providing consistent, clear, and evidence-based recommendations; communications effectively; and has navigated difficult political situations shrewdly.

Is everything okay? Still a million dollar question!

Conflict of Interest

None declared.

References

1 Rolling updates on coronavirus disease (COVID-19) updates mArch 27, 2020. Available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen Accessed April 1, 2020

2 Coronavirus disease (COVID-19) Situation Dashboard. Available at: https://experience.arcgis.com/experience/685d0ace521648f8a5beeeee1b9125cd. Accessed April 2, 2020

3 SARS-CoV-2 (COVID-19) Testing: Status Update as on March 27, 20:20 09:00 IST. Available at: https://icmr.nic.in/sites/default/files/whats_new/ICMR_website_update_27March_9AM_IST.pdf. Accessed April 1, 2020

4 Shutdown alone is not enough to break the chain, says epidemiologist Giridhara Babu. Available at: https://www.thehindu.com/sci-tech/health/shutdown-alone-is-not-enough-to-break-the-chain-says-epidemiologist-giridhara-babu/article31173750.ece. Accessed April 1, 2020

5 Cases in U.S. Available at: https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/cases-in-us.html. Accessed April 1, 2020

6 https://www.cdc.gov/media/releases/2020/s0326-nyc-truck-driver-guidance.html. Accessed April 1, 2020

7 CDC Statement on COVID-19 Apple App. Available at: https://www.cdc.gov/media/releases/2020/s0327-statement-covid-19-apple-app.html. Accessed April 1, 2020

8 CDC Statement on Self-Quarantine Guidance for Greater New York City Transportation and Delivery Workers. Available at:https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(20)30073-6/fulltext. Accessed April 1, 2020

9 The Lancet infectious disease: summary. Available at: https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30144-4/fulltext. Accessed April 1, 2020

10 Velavan TP, Meyer CG. The COVID-19 epidemic. Euro J TMIH 2020;25(3):278:280

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