



COVID 19: THE WORST HEALTH CALAMITY OF THE WORLD

Medical Science

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ABSTRACT

Infectious diseases have affected humans since the first recorded history of man. The world has experienced an increased incidence and transboundary spread of emerging infectious diseases due to population growth, urbanization and globalization over the past four decades. Most of these newly emerging and re-emerging pathogens are viruses. On an average, more than two new species of viruses infecting humans are reported worldwide every year most of which are likely to be RNA viruses. Surveillance System, early detection, identification, characterization, containment, control and ultimately prevention of the emerging infectious diseases will require a good, functional national public health surveillance system. There is an urgent need to develop a network of diagnostic laboratories, especially in countries where epidemic infectious diseases are weak. Need for real-time early detection of disease needs innovations in biomedical technology. Contact-tracking is essential. Rapid testing facilities must be available to all populations in all countries. The COVID 19 pandemic will be a definitive moment in world history and be remembered by us all. What will also be remembered is how we behave with each other. Tackling nCoV is the biggest challenge to face the World. An effective treatment and development of vaccine must be found on a war-footing.

KEYWORDS

Coronavirus, nCoV, COVID 19, Pandemic, EID, emergency preparedness, vaccine development, social distancing.

Modern civilization dates from approximately 10,000 BC. It took until 1830 for the world population to reach 1 billion persons; however, from there the world population doubled in the next 100 years and reached 6 billion 70 years after that. By the end of 21st century the world population could be between 14 and 18 billion. In the global human population, the emergence of over 335 infectious diseases between 1940 and 2014 has been reported. The emergence of these pathogens and their subsequent spread has caused an extremely significant impact on global health and economies. Humans have lived with emerging and re-emerging pathogens since before the dawn of civilization. Is the situation worse now than in past decades or centuries? The answer is probably yes because there are billions more of us and some of our activities allow such infections to appear and flourish. Moreover, our mobility within and between countries is conducive to the rapid spread of microorganisms.^{1,2}

Disease emergence is largely a product of anthropogenic and demographic changes, and is a hidden cost of human economic development.¹ New microorganisms capable of causing disease in human continue to be detected. Whether an emerging microorganism develops into a public health threat depends on factors related to the microorganisms and its environment, or the infected human and his/her environment. Factors responsible for EIDs include: microbial adaptation and change, human demographics and behaviour, international travel and commerce, economic development and land use, technology and industry, breakdown of public health measures, human susceptibility to infection, climate and weather, changing ecosystems, poverty and social inequality, war and famine, lack of political will, intent to harm, a global political commitment is rather vague.^{1,2}

A new respiratory coronavirus, 2019-nCoV, is rapidly spreading throughout world. The outbreak originating in Wuhan, Hubei province, China, coincided with Chunyun, the period of mass migration for the annual Spring Festival. To contain its spread, China adopted unprecedented nationwide interventions on January 23 2020. These policies included large-scale quarantine, strict controls on travel and extensive monitoring of suspected cases.

The COVID-19 is affecting almost all the countries around the world and 1 international conveyance (the Diamond Princess cruise ship harboured in Yokohama, Japan). The pandemic is accelerating fast. It took 67 days from the first reported case to reach the first 100,000 cases, 11 days for the second 100,000 cases and just four days for the third 100,000 cases.

According to European Centre for Disease Prevention and Control, since 31 December 2019 and as of 24 March 2020, 378 041 cases of COVID-19 (in accordance with the applied case definitions and testing strategies in the affected countries) have been reported, including 16 365 deaths. The deaths have been reported from Italy, China, Spain,

Iran, France, United States, United Kingdom, Netherlands, Germany, South Korea, Belgium, Switzerland, Indonesia, Japan, Turkey, Brazil, and many other countries.³

The percentage of health workers infected in Italy is more than double the number registered throughout the epidemic in china – more than 5000 since the onset of the outbreak in February, in part due to shortage of protective equipment.⁴

India has been placed under “complete lockdown” for the 21 days with effect from 25 March, 2020, to control community spread even as the COVID-19 positive cases are on a rise. While the governments are taking a slew of measures to ensure the availability of essential commodities in the market, Prime Minister has asked people not to panic and stay at home. The maximum number of coronavirus positive cases have been reported from Maharashtra and Kerala.

The CDC report, while specifying that in the affected U.S. population, adults aged 85 and over have the highest risk of negative outcomes resulting from the illness. The report indicates that 31% of all confirmed COVID-19 cases, 45% of hospitalizations due to the disease, 53% of admissions to ICUs, and 80% of deaths occurred among people aged 65 and over. “Older adults should: maintain adequate supplies of non-perishable foods and at least a 30-day supply of necessary medications, take precautions to keep space between themselves and others, stay away from those who are sick, avoid crowds as much as possible, avoid cruise travel and nonessential air travel, and stay home as much as possible, to further reduce the risk of being exposed.”⁵ This is the worst health calamity the world is facing since 1918-1919.

China Experience

Early data from China suggest that a majority of coronavirus disease 2019 (COVID-19) deaths have occurred among adults aged ≥ 60 years and among persons with serious underlying health conditions. COVID-19 can result in severe disease, including hospitalization, admission to an intensive care unit, and death, especially among older adults. Everyone can take actions, such as social distancing, to help slow the spread of COVID-19 and protect older adults from severe illness. It is agreed by the Epidemiologists that China's extreme lockdowns were responsible for bringing the crisis there under control. However, it is argued that if China had implemented its control measures a week earlier, it could have prevented 67% of all cases there. Implementing the measures 3 weeks earlier, from the beginning of January, would have cut the number of infections to 5% of the total.

Social distancing is recommended for all ages to slow the spread of the virus, protect the health care system, and help protect vulnerable older adults. Moreover, older adults should maintain adequate supplies of non-perishable foods and at least a 30-day supply of necessary medications, take precautions to keep space between themselves and

others, stay away from those who are sick, avoid crowds as much as possible, avoid cruise travel and nonessential air travel, and stay home as much as possible to further reduce the risk of being exposed. Persons of all ages and communities can take actions to help slow the spread of COVID-19 and protect older adults.

Impact & Implications

EIDs are a significant burden on global economies and public health. Their emergence is thought to be driven largely by socio-economic, environmental and ecological factors. EID origins are significantly correlated with socioeconomic, environmental and ecological factors. Global resources to counter disease emergence are poorly allocated, with the majority of the scientific and surveillance effort focused on countries from where the next important EID is least likely to originate.^{1,2}

Global economy is sinking and recession is a reality. The economy may be worse than what it was during the period of great depression (1929-30) or 2008-2009 global recessions. Economy may contract by at least 1%. The growth rate is expected to be just 1% for the world save China that will have it around 2%. There will be a huge gap between haves and have-nots leading to severe inequalities. Poor and disadvantaged will be worst hit. The economic effects of COVID-19 coming from reduced spending will be larger than those coming from disruptions to supply chains and illness-related workforce reductions. Such recession needs a more creative response

Globally, these are the unprecedented times, unimagined and unthought of. The deadly virus around is forcing people all over the world to make unexpected and drastic shifts in their way of life to keep themselves safe. The vital one is staying indoors, a self-quarantine measure.

More than a billion children and youth are unable to go to school because of the coronavirus pandemic. 'Education Disruption' is a phenomenon to which children and youth are wrestling since February 2020.

We cannot hope to build a better world without improving the individuals. Everybody has to work towards one's own improvement and equally share a social responsibility and response to whole humanity.

There is a dire need to stop scare-mongering and start care by connecting people who need help with people who can provide it. nCoV pandemic is knocking down whole humanity. It has debunked many modern mantras of invincible technology, scientific superpower and growth models.

The nCoV, in addition to being terrifyingly contagious, acts as an unusually merciless magnifying glass, severely overstretching our healthcare system and social safety net. It holds seriously more exact for under-developed places. So far, the handling of this outbreak has been full of failings. People are also ignoring its grave consequences.

The fight against this pandemic is a shared responsibility and everyone has to play due role in tackling the contagion.

The pandemic will change the world forever. It is argued that this pandemic will create a world that is less open, less prosperous, and less free. It could be the straw that breaks the camel's back of economic globalization.

A pandemic magnifies all existing inequalities. Working from home in a white-collar job is easier; employees with salaries and benefits will be better protected; self-isolation is less taxing in a spacious house than a cramped apartment. But one of the most striking effects of the pandemic will be to send many couples back to the 1950s. Women's independence will be a silent victim of the pandemic.

Just as this disease has shattered lives, disrupted markets and exposed the deficiencies of health systems, it will lead to permanent shifts in political and economic power in ways that will become apparent only later.

The 1930s collapse of the world economy showed how connected modern societies were and how vulnerable they were to what FDR called contagion. The United States was less threatened by other great powers than by the deep forces of modernity.

History will be written by the those who defeat the COVID-19 pandemic. Every nation, and increasingly every individual, is experiencing the societal strain of this disease in new and powerful ways. To some, this will appear as a great and definitive triumph for democracy, multilateralism, and universal health care.

This pandemic will reshuffle the international power structure in ways we can only begin to imagine. COVID-19 will continue to depress economic activity and increase tension between countries. It may reduce the productive capacity of the global economy. The risk of dislocation is especially great for developing nations and others with a large share of economically vulnerable workers. The international system is vulnerable to great pressure, resulting in instability and widespread conflict within and across countries. Many countries will have difficulty recovering.

Greatest Global Crisis

The COVID-19 pandemic is the greatest global crisis of this century affecting 204 countries. Globally, there are over 1064300 cases and 56640 deaths confirmed (as on 3 April 2020). Italy (14681), Spain (10935), USA (6605), China (3322), Iran (3294), France (5390), and UK (3605), Netherlands (1490), Germany (1210), Belgium (1143), Switzerland (573), Turkey (356), South Korea (174), Brazil (328), Sweden (360), Indonesia (170), India (72), reported more deaths than in other countries. Its depth and scale are enormous. The public health crisis threatens each of the 7.9 billion people on Earth. The financial and economic crisis could exceed in its impact the Great Recession of 2008-2009. Each crisis alone could provide a seismic shock that permanently changes the international system and balance of power. International collaboration has been woefully insufficient. In every country, however, there are many examples of the power of the human spirit—of health professionals and ordinary citizens demonstrating resilience, effectiveness, and leadership. That provides hope that men and women around the world can prevail in response to this extraordinary challenge.⁶

Education:

Though school and workplace closures have reduced the number of COVID-19 cases and substantially delayed the epidemic peak in Wuhan, China, yet it has significant negative effects on low-income families who disproportionately lack access to technology, internet, nutritious food and childcare services, as well as students with disabilities. Multiple countries successfully slowed the spread of infection through school closures during the 2009 H1N1 Flu pandemic. Mandatory school closures and other social distancing measures were associated with a 29% to 37% reduction in influenza transmission rates. School closures in response to the COVID-19 pandemic have shed a light on numerous issues affecting access to education, as well as broader socio-economic issues. By the end of March 2020, over 80% of the world's learners were impacted by closures.

Even when school closures are temporary, it carries high social and economic costs. The disruptions they cause affect people across communities, but their impact is more severe for disadvantaged children and their families including interrupted learning, compromised nutrition, childcare problems and consequent economic cost to families who cannot work. The pandemic has changed how millions around the globe are educated. New solutions for education could bring much needed innovation. Given the digital divide, new shifts in education approaches could widen equality gaps. Many countries have taken swift and decisive actions to mitigate the development of a full-blown pandemic. These changes have certainly caused a degree of inconvenience, but they have also prompted new examples of educational innovation. The pandemic can have a lasting impact on the trajectory of learning innovation and digitization.⁷

Global Response

The world has responded with unprecedented speed and mobilization of resources. The new virus was identified extremely quickly. Its genome was sequenced by Chinese scientists and shared around the world within weeks. The global scientific community has shared genomic and clinical data at unprecedented rates.

While health systems in high-income countries would be stretched by the outbreak, the most devastating effects would be in countries with weak health systems, ongoing conflicts, or existing infectious disease epidemics. In these countries, it is imperative to rapidly detect and

contain the virus at points of entry to prevent community transmission and health systems from being overwhelmed.

No antiviral treatment has been approved for coronaviruses, and despite two outbreaks of novel coronaviruses in the past two decades, vaccine development is still in its infancy. A vaccine for SARS-CoV-2 should be available sooner than later. Pandemic preparedness has become a priority for the global health agenda.

Social distancing is crucial for slowing the spread of the virus and preventing our health care system from getting overwhelmed. The pandemic is calling on us to suppress our profoundly human and evolutionarily hard-wired impulses for connection. Moreover, social distancing also tests the human capacity for cooperation. A multifarious approach is required and involvement of community leaders is critical. Responsible electronic and print media has an important role to play.

Lessons Learnt

Three countries that effectively managed nCoV disease put strong measures in place and ensured proper implementation of action plan are Singapore, Taiwan and Hong Kong. Travel restrictions, quarantines, social distancing and heightened hygiene were implemented in each country. In Singapore three university hostels were converted into quarantine facilities and people were compensated for any workdays lost. Officials then began aggressively tracing all contacts of known infected people, using data from transport companies, hotels and CCTV footage. Though large gatherings have been suspended, schools and offices have remained open to limit the outbreak's social and economic costs. However, all students and employees undergo daily health checks and temperature screenings.

Taiwan employed screened passengers on the planes after landing. It later halted flights from Wuhan and other parts of China after its first imported case. It used home quarantines more extensively than others despite availability of quarantining at state facilities. Disobeying quarantine orders also drew a penalty of up to INR 2,500,000. Mass gatherings and religious services were banned.

Hong Kong's strategy focused on limiting local transmission rather than preventing infected people from entering. It expanded its existing temperature screening facilities at entry points and asked local clinics to report any patient showing symptoms and with a travel history from Wuhan. All those crossing the border from China were placed under mandatory 14-day quarantines. Vacant, newly constructed public housing buildings were converted into quarantine facilities. Social distancing measure were extensive — large-scale events were cancelled, schools were closed until April, and civil servants have been asked to work from home for a month.

South Korea tested everyone but Italy tested only sick people. nCov cases in South Korea have dropped. It necessitates the need for increase in conducting tests. Establishing laboratory and epidemiological capacity at the country and regional levels is critical to minimize the impact of future emerging infectious disease epidemics. Improved surveillance and monitoring of the influenza outbreak will significantly enhance the options of how best we can manage outreach to both treat as well as prevent spread of the virus.

Two fundamental characteristics of microbes allow them to circumvent our attempts to control them. Whereas human generations occur approximately every two decades, those of microbes occur in minutes, allowing them to rapidly replicate. Microbes also can mutate with each replication cycle. Their ability to replicate and mutate gives them the advantage of selectively circumventing human interventions, be they antimicrobials, vaccines, or public health measures. In our battle with microbes we have an intellect and a will. We use these to implement public health measures, biomedical research, and technological advances. In essence the human species uses its intellect and will to contain, or at least strike a balance with, microbial species that rely on genes, replication, and mutation.¹²

Early detection and isolation have been the most important factors in reducing COVID-19 cases.

Emergency Preparedness

In a world of nearly 7.9 billion people, countries have to be in a state of

emergency preparedness to tackle emerging infectious diseases. Responding to the global threats of infection requires a coordinated global response with development of expertise in epidemiology, laboratory science, behavioural science, increased surveillance, adequate public health infrastructure, primary prevention and adequate communication. The best method is to bring together a diverse group of people knowledgeable about the subject of interest, provide them with good data, and ask them to imagine a series of possible scenarios. Responding to the global threats of EID requires a coordinated global response with development of expertise in epidemiology, laboratory science, behavioural science, increased surveillance, adequate public health infrastructure, primary prevention and adequate communication.

Scientists must find an effective therapy on a war footing. In these unprecedented and critical times global community has a moral responsibility to jointly fight this dreaded virus that can otherwise lead to millions of avoidable deaths. The private sector has an important role to play in efforts to fight this pandemic.

Patients who are immunocompromised make up a large vulnerable group. They are difficult to identify centrally so it will be up to us to ensure they know what to do.

Characterizing novel or re-emerging infections is aided by the availability of pathogen genomes. Genomic studies have contributed to better understanding of EIDs and their spatiotemporal spread. Sophisticated statistical methods have been developed to uncover the epidemiological features of infectious diseases based on the genealogy of their sequences. There is also growing effort to integrate genomic analysis with analysis of epidemiological data. Detecting characterizing and responding to an EID requires coordination and collaboration between multiple sectors and disciplines. Measures put in place to slow the spread of the virus may have unintended consequences by exacerbating shortages of essential protective gear, and the materials needed to make them. Solving this problem requires political commitment and political coordination at the global level. The more countries that sign up to the SOLIDARITY trial and other large studies, the faster we will get results on which drugs work, and the more lives we will be able to save. The world is rightly responding to COVID-19 with urgency and purpose.⁸

Contact-Tracking is critical to know what proportion of infected people have mild or no symptoms and might be spreading the virus. Health Care professionals are fighting an unending battle. They are our frontline warriors. Exposure to and risk of complications from nCoV is much higher in them. There is an urgent need to supplement existing number of hospitals, wards, beds, Testing facilities (laboratory equipment), human resources, Personal Protection Equipment, Staff safety checks, quarantine facilities and reporting, and all safety measure to protect the saviours and brave hearts. Director General of WHO Dr. Tedros says: 'Health Workers are heroes, but they are humans, too. They have children & families, whom they may not have seen in a while as they're fighting COVID19. They ask for our help. Their children ask for our help. StayHome'.

Critical supply shortages must be addressed on a war-footing to combat the evolving pandemic.

Emerging Perspectives for Vaccine Development

Many institutions and scientists in several countries are working day and night to find effective treatment and vaccine for COVID 19.

Most of the efforts for developing CoV vaccines and drugs target the spike glycoprotein or S protein, the major inducer of neutralizing antibodies. Although a few candidates have shown efficacy in *in vitro* studies, not many have progressed to randomized animal or human trials, hence may have limited use to counter COVID-19 infection. This article highlights ongoing advances in designing vaccines and therapeutics to counter COVID-19 while also focusing on such experiences and advances as made with earlier SARS- and MERS-CoVs, which together could enable efforts to halt this emerging virus infection.⁹

Therapeutic options that could be evaluated and used for COVID-19 include molecules binding to the virus, molecules, or inhibitors that target specific enzymes involved in viral replication and transcription, small-molecule inhibitors targeting helicase, essential proteases, or other proteins of the virus, host cell protease inhibitors, host cell

endocytosis inhibitors, siRNA, anti-sense RNA and ribozyme, neutralizing antibodies, mAbs targeting host receptor or interfere with S1 RBD, antiviral peptide targeting S2, and natural products.^{9,10}

Direct administration of monoclonal antibodies (mAbs) may play an effective role in CoV control as an intervention in exposed individuals. It has been observed that patients recovering from SARS display potent neutralizing antibody responses.^{9,11}

Technology is available for making fully human antibodies (such as human single-chain antibodies; Hu-scFvs) or humanized-nanobodies (single-domain antibodies, sdAb, VH/VHH) that can traverse across the membrane of the virus-infected cells (trans bodies) and bind to or interfere with biological activities of replicating virus proteins which consequently leads to inhibition of virus replication.^{9,12}

One antiviral-drug candidate is a combination of the HIV protease inhibitors lopinavir and ritonavir. Lopinavir, which acts against the viral 3CL protease, has modest antiviral activity against SARS-CoV-2.¹ Together with ritonavir, which increases drug bioavailability, it is in clinical trials, along with the immunomodulator interferon beta-1b, for the treatment of Middle East respiratory syndrome (MERS) (ClinicalTrials.gov number, NCT02845843, opens in new tab). What makes lopinavir-ritonavir particularly attractive is that it is widely available and manufacturable to scale and that it could be prescribed immediately. In fact, there are several case reports and case series where this agent is being used against Covid-19.¹³

Conclusion

At this moment in history we need to all work together. We need to understand which patients are most likely to benefit from ventilation so we are not offering a futile treatment. There are a bewildering number of tests becoming available and PHE are busy trying to validate them. The current test we are using in the NHS is an RT-PCR for the RdRp gene. It has a sensitivity of around 88–90%, which can be maximised if the swab is pushed right to the back of the pharynx – this is no time to be tentative. As it is not 100% sensitive keep an open mind with patients who have the typical clinical features of nCoV.

The pandemic will be a definitive moment in world history and be remembered by us all. What will also be remembered is how we behave with each other. Tackling nCoV is the biggest challenge to face the World. Health professionals are leading the fight in a war with an enemy we don't yet fully understand. The pressure will be immense. Responding to this pandemic will require us to do things differently. It will require us to be flexible. And it will require us to work right to the edge of our comfort zone, and in some cases beyond. This testing time requires us to pull together. People's individual circumstances may result in it being medically contraindicated for them to undertake front line duties but they will be able to make a contribution by carrying out duties, that support those with patient facing responsibilities. The nature of being a doctor is to go above and beyond to deliver the care our patients require. But in this crisis situation, compassion, civility, and self-care will matter more than ever. To minimize the health and socioeconomic impacts of emerging epidemic infectious diseases, major challenges must be overcome in the national and international capacity for early detection, rapid and accurate etiological identification, rapid response and effective control. Establishing laboratory and epidemiological capacity at the country and regional levels is critical to minimize the impact of future emerging infectious disease epidemics. To develop and establish such an effective national public health capacity to support infectious disease surveillance, outbreak investigation and early response, a good understanding of the concepts of nCoV is need of the hour. It seems reasonable to anticipate that within some measurable time; all the major infections will have disappeared.

Establishing laboratory and epidemiological capacity at the country and regional levels is critical to minimize the impact of future emerging infectious disease epidemics. Improved surveillance and monitoring of any outbreak will significantly enhance the options of how best we can manage outreach to both treat as well as prevent spread of the virus. Epidemic travels without passports. It kills without asking for permission, and it has done it throughout the centuries of human history. Tough times call for innovative solutions. A coordinated and committed effort is needed in at all levels to fight COVID-19. Care is above cure. Prevention is an absolute necessity. Lockdowns have to end at some point, and people should be

encouraged to maintain social distancing and good hygiene. Most vulnerable people like migrant labourers, daily-wagers, urban poor, disadvantaged, refugees, must be looked after during this pandemic. Older population (senior citizens) who feel loneliness and stress need attention.

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