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Future Perspective of Covid-19: Inevitably Becoming an Endemic

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ABSTRACT: There is a new public health crises menacing the world with the outbreak and spread of 2019 novel coronavirus (2019-nCoV) or the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Thisvirus initiated in bats and transmitted to humans through yet unknown intermediary animals in Wuhan, Hubei province, China in December 2019.The number of cases have crossed 18 crore across the world wherein the lives of around 40 lakh people succumbed to it."SARS-CoV-2", a different coronavirus, causing a prompt outbreak with a mild to moderate mortality rate. This virus is continuing to cause health care providers meriting serious considerationdue to the lack of any pre-existing immunity in the human population, indicating their novelty and lack of exposure. This raises the question is to, "Whether this novel virus will be establishing itself in an endemic form or will it eventually extinguish"? Endemic viruses while in circulation may mutate to infect ingenuous, as well as individual with previously existing immunity. Constant monitoring is highly recommended, not only to the newly infected individuals, but also to those recovered individuals who were infected by SARS-CoV-2 as re-infection may result in the selection of escape mutants and subsequent dispersion to the population. With medicines for treatment, vaccines still under stages of development, it is dreaded that now the Coronavirus pandemic is much likely to become endemic. Thereare very high chances that these novel coronaviruses could become endemic in the human population, much like influenza. If so, we could be living with COVID-19 for a long time or may be forever.

KEYWORDS: Coronavirus, SARS, COVID-19, SARS-CoV-2, pre-existing immunity

I. INTRODUCTION:

Current century appears no more an exception, the trend is continued with intensifiedscare of SARS coronavirus in 2002 and further concern of influenza H5N1 in 2003. A novel influenza virus created the first pandemic of the 21st century, the pandemic flu in 2009 led with the advent of another deadly virus, MERS-CoV in 2012.[1]

The initial wave of infection found associated with the seafood market of Wuhan, consolidating the hypothesis that close contact between the live or dead animal with an individual may be responsible for the commencement of the outbreak. In the recent past there are instances of zoonotic transmission of bird flu which directly jumped from avian species to human, but no transmission between the humans were recognized which kept the disease under control. However, the ability to spread among human to human upon close contact makes SARS-CoV-2 as a very important contagious agent to study and monitor whose desolation has already been established in Wuhan, Hubei, China. History has taught several lessons about the endemic nature of emerging viral infections. Virus faces major challenges from immunity that is already existing, to remain in the population. Other significant factors such as case fatality rate (CFR), R0 and the reservoir hosts are important in prompting viral endemicity. By analyzing CFR of different RNA viruses and their longevity in circulation throughout the globe, it was established that with higher CFR (CFR >5%), viruses die out after few passages of infections sooner or later, whereas viruses with low CFR stays endemic with a seasonal outbreak like common flu which is caused by influenza viruses. Although it is very difficult to measure actual CFR

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until the outbreak finishes, an initial estimate suggests that CFR for SARS-CoV-2 is 2.58%, much closer to seasonal flu compared to the other coronaviruses (SARS-CoV and MERs-CoV) of the recent past (i.e. 10% and 35%, respectively representing the capability of the SARS-CoV-2 to remain in circulation with low CFR throughout the world.[2]

As per the recent data, COVID-19 has already claimed 5 crore lives and more than 1 milliondeaths reported from other parts of the world.However,infected individuals already recovered from SARS-CoV2 infection, who will eventually acquire immunity to the virus.[3]

The Covid-19 recovered population increases each day, with herd immunity of the population. A virus may re-infect a person with pre-existing immunity, either in its present form (which is very unlikely), or with acquired mutations to continue in the circulation. SARS-CoV-2 recovered populations may aid the selection of mutant viruses, and their spread in the community. The World Health Organization has announced that COVID-19 will possibly never go away.This coronavirus is unprecedented in the combination of its easy transmissibility, a range of symptoms going from none at all to deadly, and the extent that it has disordered the world. Aextremelyvulnerable population led to near exponential growth in cases. At the University of Chicago, epidemiologist and evolutionary biologist Sarah Cobey says,"This is a very new anddistinctsituation,".However, past pandemics do offer cluesof the future. While there is noone historical instance to follow, humanity has gone through several large epidemics in the past 100 or so years that eventually stopped ruining society. The means they came to anend offer direction to a world looking for ways to reestablish health and some sense of normalcy. Thiswhole scenario propose that what happens next depends on both the evolution of the pathogen and of the human response to it, both biological and social.[3]

HISTORY AND BACKGROUND:

Coronaviruses and Toro viruses are two virus genera within the virus family Coronaviridae, order Nidovirales. Coronaviruses are engrained pathogens of humans and animals while the toroviruses are familiar for causingdiarrhoea in animals. Toroviruses have also been found in human faeces but their aetiological role remains indistinct.

Coronaviruses receive their name from the characteristic crown-like viral particles (virions) that dot their surface. This family of viruses infects a wide range of vertebrates, most remarkably mammals and birds, and are considered achief cause of viral respiratory infections worldwide. Including recent introduction of the 2019 novel coronavirus (COVID-19), there are now 7 coronaviruses known to infect humans:

1. Human coronavirus 229E (HCoV-229E)
2. Human coronavirus OC43 (HCoV-OC43)
3. Human coronavirus NL63 (HCoV-NL63)
4. Human coronavirus HKU1
5. Severe acute respiratory syndrome-related coronavirus (SARS-CoV)
6. Middle East respiratory syndrome-related coronavirus (MERS-CoV)
7. Novel coronavirus (COVID-19, also known familiarly as Wuhan coronavirus)

The group 1 HCoVs 229E and NL63 coronaviruses, while OC43, HKU-1 and SARS coronaviruses are categorizedin group 2. Group 3 coronaviruses are found in avian species. Genetic recombination instantlyoccurswithin the members of the same and of different coronavirus groups providing increased chance for genetic diversity. It is significant that recent studies on the comparative evolution of animal and human coronaviruses led to the conclusion that HCoV 229E and OC43, the causes of the common cold which are now globally endemic in humans, crossed species from their animal reservoirs (bats and cattle, respectively) to humans within the last 200 years, demonstrating the very fact that coronaviruses still cross species barriers and cause novel diseases.

Scientists first identified a human coronavirus in 1965. It caused a common cold. Later in same decade, researchers found a group of similar human and animal viruses and named them after their crown-likeform. The one that causes SARS developed in southern China in 2002 and swiftly spread to 28 other countries. People more than 8,000 were infected by July 2003, and 774 deceased. A small outbreak in 2004 involved only cases more than four. This coronavirus causes fever, headache, and respiratory problems like cough and shortness of breath.

MERS started in Saudi Arabia in 2012. Almost all cases of the nearly 2,500 cases have been in people who live in or travel to the Middle East. This coronavirus is less infectious than its SARS cousin but more deadly, killing 858 people. It has the same respiratory symptoms but can also cause kidney failure.[1,4,5,17,18]

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NOVEL COVID-19: Coronaviruses are a huge family of zoonotic viruses that cause wide rane of illness i.e. from the common cold to severe respiratory diseases. Zoonotic viruses have ability to transmit from animals to humans. There are quite a few coronaviruses known to be circulating in different animal populations that have not yet infected humans. COVID-19 is the most new to make the jump to human infection. Common signs of COVID-19 infection are alike to the common cold and include respiratory symptoms such as dry cough, fever, shortness of breath, and breathing difficulties. In additional severe cases, infection can cause pneumonia, severe acute respiratory syndrome, renal failure, and death.The COVID-19 infection is spread from one person to others via droplets produced from the respiratory system of infected people, often during coughing, sneezing or talking. According to data available, time from exposure to onset of symptoms is usually between 2 and 14 days, with an average of five days.[6,19]

NOVELITY OF THE VIRUS MAY LEAD TO DISASTER AND DISEASE END UP BEING ENDEMIC: A study carried out in Hong Kong at the city of Shenzhen by a group of scientistsand clinicians from the University of Hong Kong, they provided the first actual evidence for human-to-human transmission of SARS-CoV-2. This is abrilliant example of how a high-quality clinical study can make a remarkable change in policy setting. Several important clinical features of COVID-19 documented in this study.

First, an attack rate of 83% within the family context is startlingly high, which indicatesgreat transmissibility of SARS-CoV-2.

Second, the clinical manifestations of COVID-19 during this family range from mild to moderate, with highly systematic symptoms and highly severe radiological abnormalities seen in elderly patients. Normally, COVID-19 appears to be less severe than SARS. Third, child who is asymptomatic wasfound to have ground-glass opacities in his lung and SARS-CoV-2 RNA in his sputum sample. This finding of asymptomatic virus shedding increases the possibility for transmission of SARS-CoV2 from asymptomatic carriers to others.Lastly, the presentation of diarrhea in two young adults from the same family also suggests the likelihood for gastrointestinal involvement in SARS-CoV-2 infection and fecal–oral transmission. The study has set the platform for the control and management of COVID-19.[7,20]

The classification of this pandemic, as described by WHO, as a global health emergency due to its virulent nature of transmission, which may lead to acute respiratory distress syndrome. Li et al have categorically described human-to-human transmission by COVID-19 right after the respiratory droplets and environmental contamination through fomites. Within the matter of few months, the virulence of COVID-19 lead toglobal outbreak of disease, and the WHO has declared this as a public health emergency.[8]

EPIDEMIC VS PANDEMIC: To define and differentiate both is crucial for better understanding of these terms.

An epidemic is defined as an outbreak of disease that spreads swiftly and affects many individuals at the given time.

A pandemic may be a sort of epidemic which is with greater range and coverage, an epidemic of a disease that happens over a good geographical area and affects an exceptionally high share of the population.

Pandemic is less frequently encountered in a broad and non-medical sense, but does have additional senses, including “affecting the majority of people in a country or a number of countries”, “found in almost all parts of the world and in varied ecologies

PHASES OF PANDEMIC: Phase 1: None of the viruses circulating among animals have been reported to cause infections in humans

Phase 2: An animal influenza virus circulating among domesticated or wild animals is known to have caused infection in humans, and is therefore considered a potential pandemic threat.

Phase 3: This phase is characterized by animal or human-animal influenza virus has caused sporadic cases or small clusters of disease in people, but has not resulted in human-to-human transmission sufficient to sustain community-level outbreaks.

Phase 4: is characterized by verified human-to-human transmission of an animal or human-animal influenza reaffirming virus able to cause “community-level outbreaks.

Phase 5: At least two countries in one WHO region is characterized by human-to-human spread of the virus.

Phase 6: the pandemic phase, is categorized by community level outbreaks in at least one other country in a different WHO region along with the criteria defined in Phase 5

The current WHO phase for COVID-19 pandemic alert is 6.[22]

REASONS OF COVID-19 END UP BEING ENDEMIC: An infection becomes endemic when

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it remains at a comparatively constant level in a geographic area without the need for more cases to be introduced into the area. This occurs when the reproductive rate (R0) of the pathogen, in this case a virus, is essentially equal to one. The R0 is the number of new cases generated by a person who is infected by the virus and can transmit the virus to others (assuming that others are susceptible to the virus). If the value of R0 equals one then every presently contagious person will spread the virus to on average one other person. Accordingly, every time a person either recovers or passes away from the infection, another person has previously become infected. The total number of infectious people in the population in turn, remains roughly the same. An infectious disease stops spreading in an area only when the R0 stays below one. That's assuming that new cases don't come in from anywhere. The only likely way to make the R0 stay below one is to find something that can keep each contagious person from infecting on average less than one other person. This may occur if the huge majority of the people develops immunity and stay immune to the virus or if people continue to social distance for a really, very long time.[10.]

In epidemiology, there is a term called 'R0 value' (pronounced "R-naught") is known as the basic reproduction number and which accounts for expected number of cases generated directly by 1 case in a population, where all individuals are susceptible to infection. Early epidemiologic studies in the case of COVID-19 suggested an R0 value of 2.2 (90% high density interval: 1.4-3.8), which is a value similar to SARS-CoV and pandemic influenza, signaling the latent for sustained human-to-human transmission and a global pandemic.[11.]

WHAT HAPPENS WHEN A DISEASE BECOMES ENDEMIC?As per the article that was published in the journal Science, epidemic becomes "increasingly tolerated" when, they become endemic and the responsibility of protecting against it shifts from the government bodies to the specific individual. This means, the individuals takes the responsibilities for themselves for managing risk from the disease and seeking care rather than government agencies actively engaging in tracking and identifying cases.

Further, the sociopolitical response to the disease may also change, with investment in the disease becoming established along with the disease-inducing behavioural changes in people. Once people become conscious of the risks of infection, they will modify their behavior and mitigate the consequences.

Furthermore, the article suggests "owing to lack of clinical experience and knowledge also innate pathogenicity, epidemic diseases characteristically have higher morbidity and mortality than endemic diseases. Over time, effective prevention and treatment interventions appear[12]

LIVING WITH COVID-19 ENDEMIC

The statements made by WHO officials and some of the articles confirms the endemicity of the disease and if we enter this stage of disease what would be our strategy to live with Covid-19

Enlisting different approaches that help to prevent disease:

A. Protecting yourself and others from the spread of COVID-19:

a. Cleaning your hands regularly and thoroughly with an alcohol-based sanitizer or wash them with soap and water.

b. Maintain a minimum of 1 metre (3 feet) distance between yourself et al.

c. Avoid going to crowded places.

d. Avoid touching eyes, nose and mouth.

e. Use alcohol-based hand sanitizer or wash your hands with soap and water.

f. Assurepeople around you and you yourself, follow good respiratory hygiene.

f. staying home and isolating when symptoms such as cough, headache, mild fever appear, until you recover.[13.]

2. Risk reduction with additional interventions and supplements

a. Adequate sleep: Shorter sleep duration increases the risk of infectious illness. One study found that 5 h of sleep which was monitored over 7 consecutive days, increased the danger of developing rhinovirus associated cold

b. Vitamin C: Typical daily dosing of vitamin C ranges from 500 mg to 3000 mg daily with even higher doses utilized during times of acute infection.

c. Melatonin: Melatonin has been shown to inhibit NFkB activation and NLRP3 inflammasome activation. It also reduces oxidative lung injury and inflammatory cell involvement during viral infections.

d. Vitamin D: In certain conditions, vitamin D has been found to decrease NLRP3 inflamasome activation and vitamin D receptor activation reduces IL-1b secretion.

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e. Stress management: Psychological stress disrupts immune regulation and is specifically associated with increased proinflammatory cytokines such as IL-6.5

f. Zinc:COVID-19 virus appear to be susceptible to the viral inhibitory actions of zinc. Zinc could forestall coronavirus access into cells and seems to scale back coronavirus virulence.

Characteristic daily dosing of zinc is 15 mg-30 mg everyday with lozenges potentially providing straight protective effects in the upper respiratory tract.

f. Vegetables and fruits +/- isolated Flavonoids: Many flavonoids have been found, in vitro, to decrease NLRP3 inflammasome signaling, and as a result causing NFkB, TNF-a, IL-6, IL-1B and IL-18 expression. Some of the specific flavonoids which were found effective, and which can be found in the diet and/or dietary supplements include:

g. Liquiritigeninfrom Licoricedihydroquercetin and quercetin found in onions and apples. Worth mentioning, quercetin also functions as a zinc ionophore, chelating zinc and carrying it into the cell cytoplasm. This could, ideally, enhance the anti-viral actions of zinc.

h. **Myricetin** found in tomatoes, oranges, nuts, and berries

i. Apigenin (found in Matricariarecutita (Chamomile), parsley and celery.

j. Curcumin (found in turmeric root)

k. Epigallocatechinegallate (EGCG) which is present in green tea. EGCG has been found to have antiviral activity against a broad range of DNA and RNA viruses, especially in the initial stages of infection by preventing viral attachment, entry and membrane fusion EGCG, link quercetin, is a zinc ionophore, thereby potentially improving the antiviral actions of zinc.[14]

II. DISCUSSION AND CONCLUSION:

Endemicity is a definite possibility because there is no evidence that people will stayimmune lifelong or at least for a very long time after recovering from a SARS-CoV2 infection and any vaccine that emerges probably would not protect people permanently. The chances are essentially zero that everyone will get vaccinated and continue to get re-vaccinated over time to maintain protection. Ongoing anti-vaccination campaigns will work to avoid that from happening. If this virus becomes endemic, there will be some sets of questions. How usual will this infection be?What would be the percentage of the population that will get infected by the virus each year? Apparently, you want this percentage to be as less as possible. How bad will the infections in upcoming days be and what percentage of infected people will end up dying?

Currently, our immune system may react uncertainly to the SARS-CoV2 because essentially it's novel to this virus. Our immune system has never seen anything like this virus before, trying all kinds of things that donot really work and most of the first timermay become very confused. In some cases, your immune system may go erratic, actually causing lots of damage. What will happen when your immune system sees the virus for multiple times? Will it then be able to better safegaurd you? Will the resulting disease be less severe?

Then, the question arises of what could happen if the virus mutates and modifies? Your immune system may or may be unable to properly identify and respond to new versions of the virus. Endless questions

Ultimately, when the newness of COVID-19 will die down and if, in that happening, the coronavirus isn't contained or eradicated it may end up as another endemic virus that people will be exposed to in time interval.

If SARS-COV 2 does become an epidemic virus, there is no way of knowing immediately where it will be most predominant, or what the "endemicity" of disease would be?

The recent spread of SARS COV 2 has been exponentially increased with number are increasing cases day by day. Especially in country like India where population is more than 1.35 billion, virus has spread across the country. Government cannot afford to have lockdown for long, the only way for survival is to live with the virus with proper precautions, which includes wearing a mask, social distancing, regularexercises, enhancing immunity and maintaining good hand hygiene. Adopting the new way of living with precaution and simultaneously surviving with the virus just like any other virus would be the new normal. With the research is ongoing as vaccines and drugs are in trials and currently no specific treatment available. In coming days, hopefully we might get a solution to fight with the virus.

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