

Indian Perspective of Corona Virus Pandemic: In the Eyes of Internist

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Received date: June 11, 2020; Accepted date: June 26, 2020; Published date: July 03, 2020

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Abstract

The whole world is under the grasp of the on-going global pandemic of novel coronavirus i.e., COVID-19 infection. The economically stronger and more developed western countries are trying hard to cope with this health problem in contrary to these nations India is performing surprisingly well against the initial expectations. In this article we have discussed the Indian scenario of COVID-19 infection, various factors leading to the benign nature of this viral illness, and its low infectivity in India along with the advantages and flaws of various measures taken to contain this viral outbreak. We assume that the combination of various biological, environmental factors, health policies, and renovation of health infrastructure together have put India in a better position in this battle against COVID-19 infection.

Keywords: COVID-19; Lockdown; BCG vaccination; Viral outbreak pandemic

Introduction

COVID-19, the on-going pandemic is a zoonotic infectious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. Viral infections mostly tend to evolve rapidly affecting a large no. of populations within a short period. The emergence of newer viral strains makes them potential candidates to cause epidemics and pandemics [2]. Several epidemics and pandemics have been reported previously (Figure 1).

SARS-CoV-2 (also known as COVID-19) seems to be much more contagious, though unlike SARS most of the infected individuals are either asymptomatic or have mild flu-like symptoms [4].

True emergence of COVID-19 occurred late in India as compared to other western countries and in an economically developing country with inadequate healthcare facilities [0.55 hospital beds per 1000 population-2019; projected data we are facing major challenges to cope up with the situation. In this article, we will discuss clinical, demographic aspects of COVID-19 infection along with the effects of measures taken to contain the outbreak and its short/long-term impacts on the health of general Indian populations.

COVID-19 in India

The total number of cases in India has reached up to 265,819 with 7473 death and 128919 recoveries against 137608 cases including 54865 recoveries and 4004 death till 24th may with relatively lower case fatality rate (2.81% against the global 6.62%). Clinical features of COVID-19 infection may range from asymptomatic carriers to severe acute respiratory illness and most severely affected cohorts are elderly population especially those with comorbidities [3]. Most cases are either asymptomatic or with mild flu-like symptoms (International Pulmonologist's Consensus on Covid-19) not requiring hospitalization but isolation. Severe lung involvement causes ARDS like symptoms for which ICU admission and ventilator supports are warranted. Better patient characteristic delineation in India will be possible with case reports and case series analysis.

At the very beginning, it was speculated that a large number of Indian population will get infected with COVID 19 over due course with a higher mortality rate as compared to western countries. Whereas in the present scenario India seems to have made it possible to contain COVID-19 infection to a large extent. The positive cases of COVID-19 seem to be lower in India as compared to other countries like the USA, Italy, Spain, the UK and many of us seem to relate it to the lower testing rate in India. Initially in India only symptomatic, high risk and those with positive travel history were being tested although the later on the more rapid testing policy was adopted. If we assume

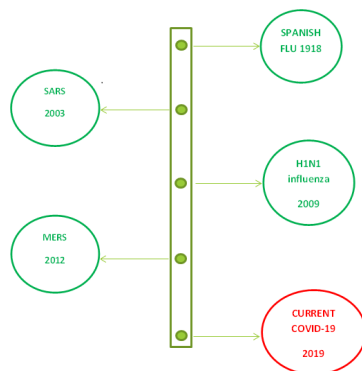


Figure 1: Previous important viral outbreaks.

The genomic sequence study of the causative agent of this recent outbreak i.e SARS-CoV-2 has shown around 96.2% similarity to bat CoV genome and 79.5% similarity to SARS-CoV [2,3]. Based on this analysis bat has been suspected as the natural host of the virus transmitting it to humans from an unidentified intermediate host. During the SARS-CoV outbreak in 2003 around 8000 individuals became infected and it was possible to contain the infection with general infection control measures [2,3]. On the other hand this new

these suspected cases as the tip of iceberg, then also we can further comment that the severity of COVID-19 related illness is much less as compared to western countries. The index case in India was a medical student who returned from Wuhan and was diagnosed on 30th January 2020 in Kerala [4]. In the next 4 weeks cases rose to 44 with an exponential rise as shown in the diagram (Figure 2).

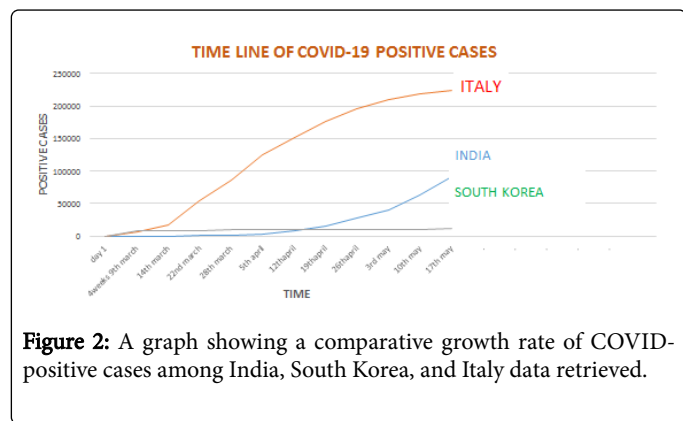


Figure 2: A graph showing a comparative growth rate of COVID-positive cases among India, South Korea, and Italy data retrieved.

1st case in Italy also was reported at the around same time on 31st January but the rise of cases in the next 4 weeks in Italy showed a relatively rapid spike. As compared to Italy countries like South Korea showed much less spike in positive cases even though both had adapted rapid testing policy (Table 1).

Hence aggressive testing did not seem to affect the number of positive cases as seen in India and South Korea; this leads the experts to believe that many other factors are contributing to this low infectivity in India apart from lockdown and social distancing alone. Based on this, experts hypothesize a few factors to be responsible for this low incidence of COVID-19 in India amongst which are environmental, biological, and medical factors that influenced this flattening of the curve in India as compared to other more developed countries where aggressive testing is being carried out [4,5].

| Country | Population | Tests done | Positive result | % of positive result against total testing | % of positive result against total population |
|-------------|------------|------------|-----------------|--|---|
| INDIA | 1378418813 | 2943421 | 137608 | 4.67 | 0.00998 |
| ITALY | 60471682 | 3391188 | 229327 | 6.762 | 0.3792 |
| SOUTH KOREA | 51264240 | 820289 | 11190 | 1.364 | 0.0218 |

Table 1: Country-wise distribution of total population, number of testing done, positive result (absolute value and % value concerning population and number of tests).

Effect of Medical Policies

The difference in the intensity of COVID-19 cases in India compared to other developed countries is being linked to the practice of universal BCG vaccination for all new-borns in India. India started it in 1949 and around 97% of the 26 million Indian children born received BCG vaccination last year [6]. Sharing the border with China and being the 2nd most populous country with inadequate healthcare facilities we were expected to have a much higher number of cases with higher mortality rates, in contrary to this relatively lower incidence rate with a slower rise of positive cases in India could be partly attributed to the BCG vaccination status also observed with many other countries [7]. An epidemiological study showed that countries without universal BCG vaccination (Italy, Netherlands, and USA) showed more number of positive cases and higher mortality compared to countries that adopted universal immunization policy with inclusion of BCG vaccination like India, Japan [7].

Non-specific immune effects or positive heterologous effect is the property of many vaccines that we use and this very effect of BCG vaccine is responsible for immunity against non-mycobacterial pathogens [7,8]. It increases the release of pro-inflammatory cytokines like IL-1B, which is an important cytokine with antiviral property [9-11]. This non-specific effect is also related to decreased incidence of sepsis and upper respiratory tract infection in people who received BCG vaccination.

An epidemiological study (Aaron Miller et. al.) observed that middle and high-income countries with and without universal BCG vaccination policy have a significant difference in both mortality and incidence of COVID-19. Countries with BCG immunization policy showed a mortality rate of 0.78+0.40 deaths per million people and 59.54+23.29 (mean+s.e.m) cases per million inhabitants, in contrary to countries with no policy showing 16.39 ± 7.33 deaths per million people and with 264.90 ± 134.88 (mean+s.e.m) cases per million habitats [7]. This analysis suggests that BCG vaccination might provide long-lasting immune effect against current coronavirus strain, though this warrants further clinical studies to establish the relation. There are various on-going randomized controlled trials on related topics (like in Netherlands, Australia-NCT04327206, NCT04328441) results of which might provide more insight on this postulated correlation. WHO addressed various confounding factors in those studies which showed a positive correlation, hence no change has been made in BCG vaccination policy till further evidence is there [8].

Environmental Factors, Meteorological and Population Density Factors

Meteorological factors play an important role in the spreading or containment of infectious diseases. As a zoonotic disease COVID-19 is transmitted from animals to human beings through an unknown intermediate host or direct transmission (lack of clear cut evidence) and with time it is evident that there is the human to human transmission. The global spread is aided by movement and crowding

making it very clear that population density is an important considering factor [7,12]. Due to its highly contagious nature and rapid spread, environmental factors also play an important role along with population density [12,13].

Being the 2nd most populous country in the world with a population density of 464 per Km² (<https://www.worldometers.info/world-population/india-population/>) number of cases in India should have been more because of the high transmission rate of such communicable diseases among those living in crowded conditions as compared to low population density countries like Italy, USA is again in contrary and explanation to this paradox needs further studies.

India being in a tropical climatic zone has dry and humid climatic conditions, which again plays an important role in viral transmission [14]. A study by Yueling et al. showed that an increase in absolute humidity led to a decrease in corona virus-related deaths in China [12,13].

Biological Factors

SARS-COV-2 is a positive sense, enveloped, RNA genome of 29.9 kb [3,15]. There are around 4 genera in coronavirus: α , β , γ , δ , among these 4 genera, 6 CoVs were identified as human-susceptible viruses previously [3,16] α -HCoV-229E, α -HCoV-NL63, β -HCoV HKU1, and β -HCoV-Oc43 are known to cause mild upper respiratory illness in humans. Rest of the two beta corona virus-SARS-CoV, MERS-CoV cause fatal respiratory illness [3,17] (Figure 3).

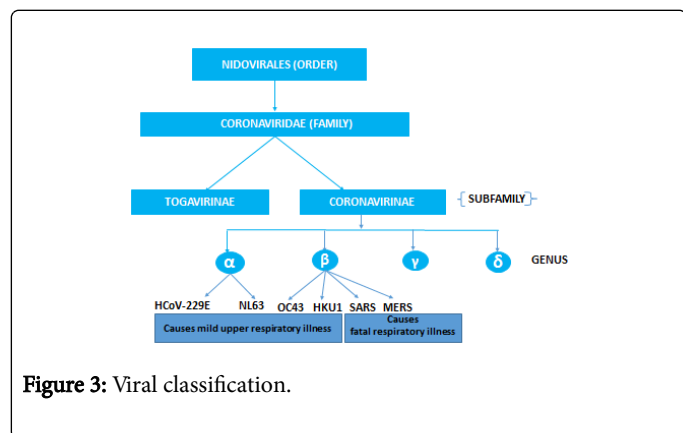


Figure 3: Viral classification.

Wu et al. [17] showed that there is a polygenetic and genomic similarity between SARS cov and SARS-Cov-2 especially in S glycoprotein.

ACE-2 is the only known receptor of SARS-CoV, found in many cells of human bodies especially the respiratory tract and mucosa of the gastrointestinal system. Zhou et al. [18] showed that SARS-CoV-2 also uses the same cellular entry as SARS CoV as seen while testing BAL fluid of COVID-19 patients. The S protein binds to the ACE 2 receptor releasing viral RNA into the cytoplasm following which the replication of the virus starts simultaneously stimulating the defence mechanism of the body leading to cytokine storm and further clinical manifestations [3]. The receptor responsible for attachment and entry of virus i.e., ACE-2 shows many polymorphisms that may increase or decrease the virus binding and entry leading to variation in clinical manifestations. Polymorphism of ACE 2 might be responsible for different clinical phenol typing of COVID-19 infections and their role as a potential therapeutic target should be explored by further studies [19-22] (Figure 4).

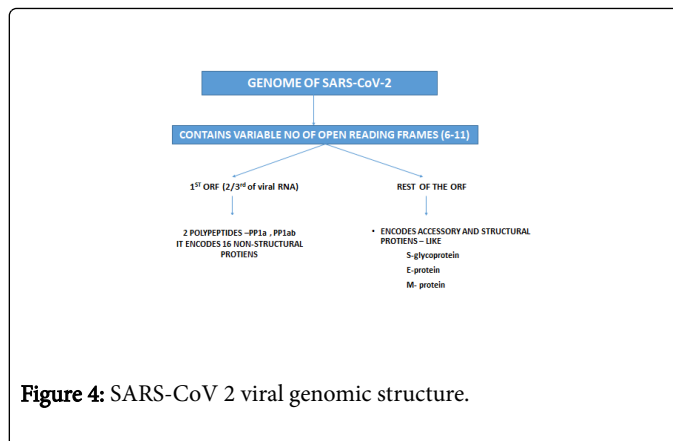


Figure 4: SARS-CoV 2 viral genomic structure.

Lockdown and its Effects

As the COVID-19 epidemic surfaced in many countries following which WHO declared it as a pandemic many steps have been taken by our government officials like – social distancing, thermal temperature monitoring at airports, restriction on movement of people from other countries and quarantine measures for Indian nationals coming from other countries. Apart from these the major step taken by our govt. is nationwide lockdown in phases starting from 25th March 2020 till date.

The Lockdown measures per se might not reduce the total number of cases but breaking the chain of transmission can have a great effect on the speed at which the spread of COVID-19 occurs hence providing the system with time to strengthen its facilities preventing overflow of cases in hospitals (Figure 5).

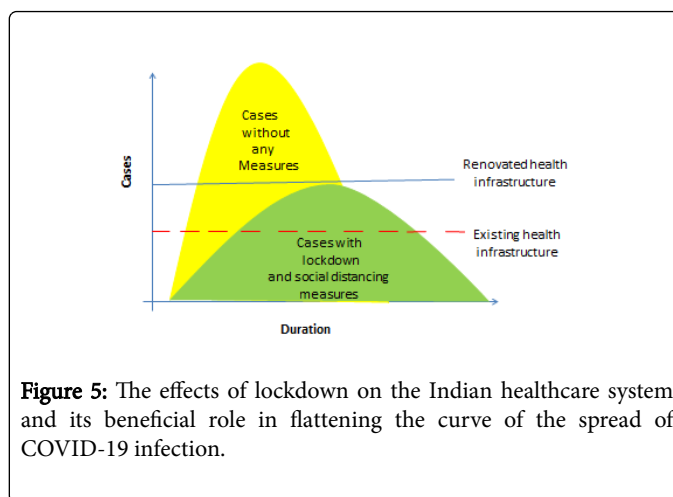


Figure 5: The effects of lockdown on the Indian healthcare system and its beneficial role in flattening the curve of the spread of COVID-19 infection.

Relatively rapid rise of positive cases after relaxation of lockdown during first week of June supports our hypothesis. In a country with inadequate health-care facilities lockdown plays a very crucial role especially in the initial few days. Though to suppress the curve lockdown alone cannot help, measures such as contact tracing and isolation play a very important role. Initially as a part of pandemic preparedness, this big decision of this countrywide lockdown taken by our govt. was an appreciable approach though short and long term effects of this stepwise prolongation of lockdown is a matter of debate.

Most of the viral infections are self-limiting. Other possible ways to get rid of viral infections are specific vaccination, antiviral drugs, and the development of herd immunity. By means of lockdown we are trying to escape the viral attack and it will help us to some extent by giving time to be prepared though, in the long run, this might be inadequate as herd immunity development will be delayed and in a short time, most of us will get infected once lockdown is withheld unless the specific vaccine is available.

There are various other effects of lockdown. Prevalence and Mortality rate of other chronic diseases like tuberculosis are much higher in our country. As a major portion of our existing health care facilities has been directed to take care of COVID-19 related issues normal care of other diseases is being hampered adding to it also lack normal transport facilities has led to OPD follow up of these patients very difficult. The psycho-social effects of lockdown cannot be ignored. Front-line health care professionals are working under stressful conditions. Restricted movement is creating undue mental pressure amongst the general population. Economic loss during covid-19 outbreak might have significant short and long-term impact on health of general population.

Preparedness in India to Combat COVID-19

For the last few months India is trying to fight COVID-19 pandemic with great preparedness. Most of the institutions have prepared their protocol based on available and newly published national international guidelines. Separate facilities for COVID-19 have been made, protective gears are being provided to frontline warriors, the number of testing and policy of contact tracing is being strengthened every day. Testing criteria are being updated regularly and a lower threshold for testing is being implemented. Various temporary isolation and quarantine centers have been prepared to prevent overflow of patients at tertiary care centers. The availability of more number of ventilators has been ensured at appropriate centers. Multimedia campaigning, online panel discussions have created greater public awareness. The adoption of the online smooth reporting system and advanced technology has made the contact tracing easier. Different states across countries have adopted different strategies to battle COVID-19 like Kerala's policy of extensive testing, contact tracing, and community mobilization by their previous experience with Nipah virus, 2018. Odisha has channelized their hands on experience of natural disaster management towards COVID-19 preparedness. Government and private sectors are trying for maximum usage of technology in this era of lockdown like drone-monitoring of physical distancing at Mumbai, development of remote health monitoring devices at AIIMS, Rishikesh in collaboration with Electronics Corporation of India Limited (ECIL) [22]. Biomedical researches are going on towards the discovery of a vaccine. Although hydroxychloroquine showed conflicting results for prophylaxis as well as treatment of COVID-19 cases, its widespread availability has been ensured in India along with antiviral drugs. Biological agent, tocilizumab (IL-6 inhibitor) was approved in china for the treatment of severe COVID-19 patients based on positive results on a small number of the study population, but the cost and availability of this drug remains issues in India. Various experimental treatment strategies (like plasma therapy) and drug trials (like tocilizumab, interferon alfa) are being conducted at the institution level across the country.

Conclusion

The COVID-19 infection rate in India seems to be low compared to as expected initially. This could be attributed to the timely announcement of lockdown, various environmental and biological factors along with health-care policies. The real-life scenario will be clear once the lockdown is withdrawn. As of now, the only possible way to get rid of this mighty virus is the early development of adequate herd immunity. So, undue prolongation of lockdown might not help us much in the long run. The balanced approach is the need of the hour. Strengthening of existing healthcare facilities time for which the lockdown has already provided and gradual relaxation of lockdown will be a welcome approach in this regard.

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