Why India may do much better off with COVID-19

Dr. Rajender Singh

Principal Scientist

CSIR Central Drug Research Institute, Lucknow, India

Lucknow, UP, India

E-mail: rajender_singh@cdri.res.in

Citation: Rajender S. Why India may do much better off with COVID-19. Polymorphism. 2020; 4: 53-58.

Viruses are submicroscopic organisms, which have minimal cellular machinery and are dependent upon the host for their multiplication. They hijack the host cellular machinery to synthesize proteins necessary for their survival and replication, ultimately killing the host cell and bursting out in large numbers. This is also the key to their survival inside the host as their hiding inside the cells does not let the immune system to clear them off easily. Various pathogenic invaders are cleared from human body by B and T cells, which act in coordination with each other. As we survive amid a variety of organisms, nature has equipped us with a battery of genes and mechanisms that can tackle virtually any pathogen we may encounter. Apart from a variety of mechanisms that make it possible, the immune system is equipped with a unique and continuously evolving mechanism of class-switching to fine tune the response to its best efficacy depending upon the requirement (Chaudhuri et al., 2007).

However, sudden outbreaks of new viruses as a result of zoonosis may give us a tough time before our immune system learns how to tackle them. In the ongoing worldwide pandemic of Covid-19, more than 800,000 people are already infected and more than 40,000 have already succumbed to this virus (https://www.google.com/covid19-map/). The first case of Covid-19 appeared in China in November 2019, which later spread to almost every country in the world with Italy, Spain and USA being the worst hit (WHO). Today USA tops the world in the number of infections and US CDC estimates that the death toll in USA could be as high as 100,000 to 200,000. A number of developing countries including India have seen much lesser number of infected cases in comparison to many developed countries (Fig. 1, Table 1). As far as India is concerned, I believe that Indians may do much better off with battling Covid-19. I propose this on the basis various perspectives with relevant scientific hypotheses.

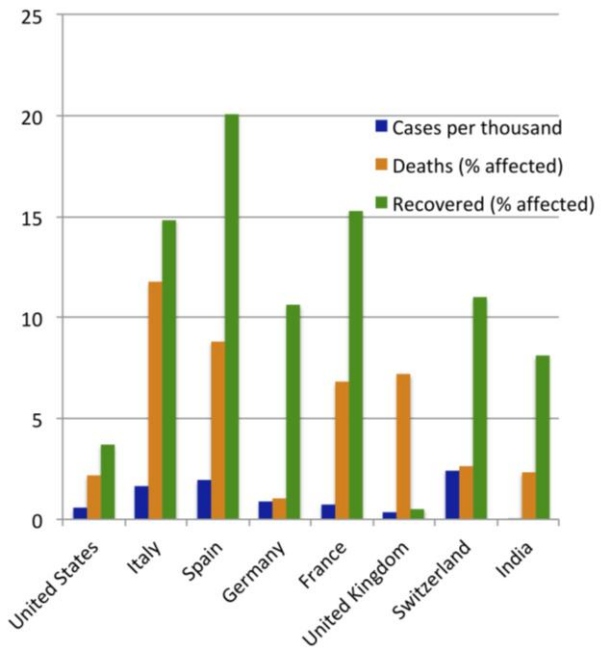

Fig. 1. Comparison of the number of infected cases, recovery rate and death rate across countries. Data only for the countries in log phase of infection are included and the data for China has been omitted as they have already declared the end of this infection in their country. The data is as on 1st April, 2020, derived from Wikipedia.

Table 1. COVID-19 data as on April 1, 2020*			
Country	Cases per thousand	Deaths (% affected)	Recovered (% affected)
United States	0.577	2.15	3.7
Italy	1.675	11.74	14.86
Spain	1.936	8.8	20.08
Germany	0.875	1.07	10.63
France	0.762	6.8	15.31
United Kingdom	0.388	7.19	0.54
Switzerland	2.445	2.6	10.98
India	0.0011	2.3	8.12

* This table represents the same data as shown in Fig. 1. It is added only for the purpose of clarity and comparison.

Since India saw the first case much later than China and Italy, it helped the government learn a lot and impose lockdown quite early in comparison to other countries. This must have aided in reducing the spread of the infection by asymptomatic people. Today during the period of lockdown, there is fear even in the illiterate population and a large section of the educated or uneducated society is following the lockdown. While it may be easier to spread knowledge in societies with high literacy rate, relatively less literate population is also following the lockdown due to the inevitable fear in the lack of knowledge. The overall result of the efforts of government and the response from people may be evident in very slow doubling of the cases. According to Corona data from various online sources, India is second slowest country with respect to the doubling time of the cases.

The major factor is with respect to the evolutionary fitness to tackle viral infections. Every species rides the wheel of evolution in a constant endeavor to improve its fitness and ensure its survival. This is catered in the form of continuous evolution to better evolve the genetic material, which is more robust and resistant to perishing. Charles Robert Darwin, with a M.A. degree in theology and an unquenchable thirst for natural history, proposed the theory of natural selection in his famous book, Magnum Opus, published in 1859. The core of the book states that life forms are mutable and new and complex forms of life are created by mutations and natural selection. The beneficial changes that provide an edge are selected and propagated while those with negative impact are eliminated in the competition for survival. No doubt, change is inescapable truth of life and nothing in biology makes sense except in the light of evolution.

In developing countries with a huge population like India, there are a number of prevailing infections that are relatively less common or not seen in the developed countries. In India, there are at least 2-3 seasons ever year when people catch a variety of flu: influenza, dengue and chikungunya, among other infections. The prevalence of these infections must have put humans under selective pressure, resulting in the selection of genomic variations that make them better fit to handle such infections. Further, while flu vaccine is available and is invariably used across a number of developed

countries, it is neither included in the national healthcare programme nor considered to be essential by most Indian people. This leaves the natural system to handle the infections in the natural way, resulting in selection pressure on immunity genes. This may explain lesser number of infections, low level of morbidity and lesser percentage of deaths due to COVID-19. Since there is no data with respect to the level of morbidity, particularly the length of infection in infected individuals and the level of medical aid required to manage the patient, collection of such data would provide further clues to this proposal.

In the pursuit of natural fight for survival, both humans and viruses mutate, interact and evolve. The co-habitat of both these in developing countries leaves humans with no other mechanism but to continuously interact and evolve. In the developed world with lesser burden of viral diseases, the evolutionary pace to betterment with respect to the viral diseases may also be low. In such a scenario, the introduction of a new virus can create havoc in populations less fit to tackle viruses. A number of viruses such as dengue and chikungunya are now permanent residents in some of the developing countries, including India, which return to cause infections every year (Kumar et al., 2017; Mourya et al, 2019). This is equivalent to natural repeated immunization in these populations, which might show some cross-reactivity with new viruses.

In the midst of COVID-19 pandemic, there are reports that BCG vaccine, which is given in many countries including India, could have some beneficial effect. The only similarity between COVID-19 and tuberculosis is that both affect lungs, otherwise the biological organisms causing the two are entirely different. In the lack of a concrete evidence favoring protective effect of BCG vaccine, I see this as a coincidence, which may actually derive the linkage of less number of infections in these populations to their genetic makeup that has evolved over the years to tackle viruses in a much better way than others who do not encounter viral infections so often and with high diversity. Nevertheless, a clinical trial on trying BCG vaccine for frontline health-workers has already been registered (Clinical trials registry, clinicaltrials.gov).

The evolutionary fitness of a genome to tackle viruses or any infection can be tested in migrant workers. USA and Italy are now the epicenters of Covid-19. There were at least 170,000 Indians in Italy in the year 2016 and at least 44,00,000 Indians in USA in the year 2018. It would be very interesting to see the infection rate, morbidity and mortality in the people of Indian origin in these virus-hit countries. The data from migrant populations become quite interesting as they live in the same environment with genetically different populations, providing a good opportunity to study the genetic contribution to their immunity to certain pathogenic outbreaks.

The third factor could be environmental,

particularly solar heat and radiations. UV radiation from the sun is the primary germicide in the environment. Almost all viruses are sensitive to UV radiations from sun (Lytle and Sagripanti, 2005), though the sensitivity varies and SARS-CoV2 remains to be tested for its sensitivity. Viruses in general survive better in low temperatures. It has been found that SARS CoV can survive in environment for over 5 days at temperatures of 22–25°C and relative humidity of 40–50%. This is the condition of typical air-conditioned environments. However, virus viability was rapidly lost at higher temperatures and higher relative humidity (e.g., 38°C, and relative humidity of >95%) (Chan et al, 2011). India would see temperature above 40°C after April 15 and heat and UV radiation may reduce the spread of the virus. Nevertheless, it must be born in mind that since the virus spreads by contact, the lockdown and social distancing would still be required to take full advantage of hot climate and to completely eliminate the virus. A number of tropical countries have relatively low number of active COVID-19 infections, which could be due to climatic conditions unfavorable to the virus. With the onset of summer, the infections should decrease further. There are apprehensions in the scientific fraternity with respect to the effect of high temperature on this new virus, but given the general susceptibility of viruses to high temperature, the plausibility of its effectiveness seems quite high.

Another interesting phenomenon that must be kept in mind is new mutations in viruses as they evolve rapidly. Genome sequencing across affected countries has already shown that virus RNA sequence across these countries, including India, differs to some extent. A recent systematic gene level mutation analysis study from India found a unique mutation in the spike surface glycoprotein (A930V (24351C>T)) in the Indian SARS-CoV2, which was absent in strains from Wuhan, Italy and USA (Sardar et al, 2020). This study also identified a host has-miR-27b, which had a unique target in Indian SARS CoV2 genome only. The contribution of these viral genomic variations to their virulence could also account for some of the differences in its pathogenicity, morbidity and mortality in various countries. Nevertheless, new mutations can also lead to a more virulent strain of the virus, making it difficult to account for their contribution in slowing the infection. Moreover, several strains of the virus may co-exist in a country, each with a different level of morbidity and mortality.

My proposal has certain limitations. In the lack of relevant scientific epidemiological data, most of the data presented in this article is based on various online sources, which are secondary in nature and significantly prone to errors. One may argue that India and other developing countries are not testing enough number of individuals. While this may have substance, it does not affect my proposal. Even if there has

been a lack of testing, the number of deaths in these countries would suddenly jump if the infections were widespread despite low testing rate. Additionally, the average age and the health scenario of the population of a country may have a significant impact on the morbidity and mortality. Over and above this, the number of deaths in a particular country could be significantly affected by the availability and the standard of medical facilities. The above hypotheses may apply to many other developing countries, particularly in the temperate zone, if high temperature also makes a significant contribution.

DISCLAIMER

The opinion expressed in this article is author's personal view and not necessarily that of his institute.

REFERENCES

Chan, K. H., Peiris, J. S., Lam, S. Y., Poon, L. L. M., Yuen, K. Y., & Seto, W. H. (2011). The effects of temperature and relative humidity on the viability of the SARS coronavirus. Advances in virology, 2011.

Chaudhuri, J., Basu, U., Zarrin, A., Yan, C., Franco, S., Perlot, T., .. & Manis, J. (2007). Evolution of the immunoglobulin heavy chain class switch recombination mechanism. Advances in immunology, 94, 157-214.

Clinical trials registry. https://clinicaltrials.gov/ct2/show/NCT04327206. Accessed on April 1, 2020.

Coronavirus disease (COVID-19) Pandemic. https://www.who.int/emergencies/diseases/novel-coronavirus-2019. Accessed on April 1, 2020.

Google Corona map. Available at: https://www.google.com/covid19-map/. Accessed on April 1, 2020.

Mourya, D. T., Yadav, P. D., Ullas, P. T., Bhardwaj, S. D., Sahay, R. R., Chadha, M. S., et al. (2019). Emerging/re-emerging viral diseases & new viruses on the Indian horizon. The Indian journal of medical research, 149(4), 447.

Kumar, P. S. S., Arjun, M. C., Gupta, S. K., & Nongkynrih, B. (2018). Malaria, dengue and chikungunya in India–An update. Indian Journal of Medical Specialities, 9(1), 25-29.

Lytle, C.D., Sagripanti, J.L. Predicted inactivation of viruses of relevance to biodefense by solar radiation. J Virol. 2005 Nov;79(22):14244-52.

Sardar, R., Satish, D., Birla, S., & Gupta, D. (2020). Comparative analyses of SAR-CoV2 genomes from different geographical locations and other coronavirus family genomes reveals unique features potentially consequential to host-virus interaction and pathogenesis. bioRxiv.

Wikipedia Corona statistics page available at. https://en.wikipedia.org/wiki/2019%E2%80%9320_coronavirus_pandemic_by_country_and_territory. Accessed on April 1, 2020.