Coronavirus (SARS-CoV-2) and Mortality Rate in India: The Winning Edge

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The Covid-19 outbreak is due to a virus which emerged in China at the end of December 2019, and is now widespread in more than 200 countries worldwide (1). Several researches have highlighted that it was introduced to humans from bats (2, 3). The infection spreads like a chain reaction as one infected person passes this virus to two or three others, who then continue to spread it in a similar manner (Figure 1). The number of people infected in a region from a single person is estimated as $R_0$ (R zero). $R_0$ is the rate at which new infections stem from a single case (4). $R_0 < 1$ indicates the reduction of cases, whereas $R_0 > 1$ suggests that the number of cases are increasing. The global $R_0$ value for Covid-19 is estimated to range between 3 and 5, which is twice as fast as SARS (Severe Acute Respiratory Syndrome) (5). This is why the spread of Covid-19 is so rapid, and why the number of infected people double every 5–10 days (Coronavirus in India). The socioeconomic impact of Covid-19 is disruptive, and the whole world is looking forward to the end of this crisis. Similar to other countries, its transmission among the Indian population is evident. But the major question is its fate in India, as India makes up one-fifth of the world's population. The recent report makes India's fate more vulnerable, by estimating that the total number of reported cases are 10-fold less than the total number of infected people (6). Thus, such complexity makes India one of the most monitored countries during this pandemic.

Contrary to what one would expect, the emerging data suggests that at the front of mortality, the situation in India turned out not to be as bad as in some European nations and the USA. However, given the fact that India's emergency services are limited, it is likely to be more vulnerable to this pandemic. Keeping this in mind, the Indian government has introduced unprecedented measures (including the stringent and early nation-wide lockdown from March 22), to stop the spread of Covid-19. Wherever a high number of cases are found, it is considered as a hotspot. The locality is immediately sealed to stop the spread of the virus. Further, in lockdown 3.0, the country was divided into green, orange, and red zones, based on severity and the number of cases (MOHFW-GoI)1. However, we are not sure how long this measure should be implemented and what the chances of resurgence will be when these restrictions are relaxed after a few weeks. Equally at the research front, scientists from all over the world are trying to find a way to exit from this crisis. More than 20,000 research papers (doubling every 20 days) on this topic itself suggests its seriousness (7). Indeed, social distancing and other governmental measures would reduce the virus's ability to sweep through the population, but unless, or until a vaccine is discovered, what measures can India rely upon to control the spread of the virus?

The one and most prominent way is to obtain “herd immunity” (8). When a population is exposed to any infectious disease, many of its inhabitants gain immunity in a short period of time. When ~70% of individuals in the population become immune, this facilitates herd immunity. This barrier of immunity blocks the virus from taking hold and infecting others. Immunity may be sustained for almost a year, and such a time period can buy us time to develop a vaccine. Moreover, immune people can volunteer for the healthcare services and other necessary activities without any sophisticated protective gear. This seems easy to implement, but when looking fatalities figures for

1Available at: mohfw.gov.in.
the coronavirus, we cannot put the life of ~3% (or even more) people on the line (Figure 2A). Therefore, thinking of obtaining rapid herd immunity in this particular case, is an autophagy for a nation like India. A recent example is the UK, which had initiated this method in the beginning as a measure, but seeing the severe impact of the virus, abandoned this plan (9, 10).

Accumulating research in other regions of the world are suggesting the effect of high temperatures and humidity on Covid-19 (11–13). However, so far, none of the dedicated studies in India have been performed on the association of temperature or humidity on the spread of Covid-19. Therefore, the relevance of temperature on the spread of Covid-19 in India is not known.

Recent research suggests that the coronavirus receptor of human ACE2 plays a pivotal role in disease predisposition, therefore, certain polymorphisms in this gene may affect the susceptibility of a population (14–21). As an expert on Human Evolutionary Genetics, it is necessary to reiterate that, in India, modern humans have been living for at least 50,000 to 70,000 years and have experienced various kinds of pathogen pressures (22–25). A large number of genetic and archaeological studies are consistent with a largely local emergence of South Asian ancestry with minor [and in some cases relatively higher e.g., Tibeto-Burmans (26), Austroasiatics (27), and some Northwest Indian populations (28)] ancestry contributions from East and West Eurasians respectively (29–31). Therefore, these long term geographic and genetic isolations, might have certainly helped us to modify our genetic landscape against various kinds of pathogens (22, 25, 32–34). Moreover, the high level of endogamy practices among caste and tribal populations (29, 35) has created a unique genetic profile, and thus, likely variations in ACE2. Therefore, it is likely that many of the endogamous populations might have developed a varied degree of susceptibility responses against this virus.

FIGURE 1 | The graphical representation of Covid-19 infection in a natural population. The viral infection spread from peer-to-peer like a chain reaction. This figure is only a graphical representation of the spread, without considering whether someone in the population has recovered or died.
In fact, Cao et al. (15) have looked at the binding sites of the S protein of coronavirus but did not find any variation among 1,000 genome populations. However, keeping in mind that 1,000 genome South Asian samples do not capture the complete South Asian diversity (36), one should look at these variations as well as whole ACE2 variations in the large number of South Asian ethnic groups. Moreover, the greater role of ACE2 in disease manifestation is evident in our recent study, which showed that the major South Asian ACE2 haplotypes are identity by descent (IBD) of East Eurasians rather than West Eurasian (19), which is possibly one of the reasons for the low mortality among the Indian population. Therefore, studying the detailed ACE2 variations among diverse Indian populations would be worthwhile to understand human susceptibility to Covid-19.

A study done by the Chinese Centre for Disease Control and Prevention on 72,314 cases suggested the presence of 1% asymptomatic individuals (Chinese Center for Disease Control and Prevention)2. Asymptomatic individuals are people who have been diagnosed to have a positive viral load but lack any characteristic symptoms including fever, dry cough, and fatigue etc. Recent data in India has identified 28% asymptomatic people—which is alarming (Figure 2A). Notably, ~65% of the Indian population is under the age of 35 years, thus the number of asymptomatic people would likely be much higher than reported (6). Therefore, it is highly alarming and brings to the forefront the question—how can one stop infections that are spread by asymptomatic people?

To identify asymptomatic people, two important dependent measures can be applied. First is mass antigen/antibody testing, and second is to look at their ACE2 variations. In order to investigate the real spread estimation (6), as

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FIGURE 2 | The analysis of Covid-19 from India. (A) The frequency (%) of infected people with various levels of symptoms. The data was obtained from (https://www.mohfw.gov.in/). (B) The statewide mortality rate (number of people deceased/total number of reported cases) of the infected people. The data was obtained from the https://www.covid19india.org/ and plotted through (https://app.datawrapper.de/). (C) The mortality rate of India in comparison with the USA, the UK, and Italy. (D) The plot of day-by-day recovery rates (number of people recovered/total number of reported cases) in India (last updated: 12th May 2020). The data was obtained from (https://www.mohfw.gov.in/).

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2http://www.chinacdc.cn/en/COVID19/ (accessed March 29, 2020).
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Conflict of Interest: The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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