COVID-19

Tuberculosis-prone countries and resistance to COVID-19

Prasanta Kumar Ghosh

Ex-Adviser, Department of Biotechnology, Ministry of Science and Technology, Government of India, New Delhi, India

Abstract

The severe acute respiratory syndrome coronavirus 2 (SARS CoV2) also called human coronavirus 2019 (HCoV-19) causing COVID-19 flu originated from China. The complete nucleotide sequence of SARS CoV2 was revealed in January 2020 by Chinese scientists, opening up opportunities for developing therapeutic agents and vaccines. The Chinese people were late in declaring the onset of the disease; only during January 2020, it was revealed that this disease was spreading like an epidemic from man to man contact. The spread of the disease and deaths, in the meantime, were very high in a short period all over the world from man to man contact. To prevent these, use of masks, social distancing among the noninfected and maintaining isolation in houses for a period to allow the surroundings to get absolved from infection, and locking down the infected in hospitals or at home with supportive therapy were effective to prevent the spread. Current country-wise world data on diseased individuals and the deaths reveal that the developing countries having a preponderance of tuberculosis perform better in comparison, to resist the disease with concomitant lesser deaths. The efforts of developing an effective vaccine would require a painstaking, precise understanding of the manner the virus mutates and mount vaccination strategies to effectively neutralize and opsonize.

Keywords: Coronavirus, developing countries, tuberculosis

Address for correspondence: Dr. Prasanta Kumar Ghosh, Ex-Adviser, Department of Biotechnology, Government of India; Block: C2B, Flat: 5A, Janakpuri, New Delhi 110058, India..
E-mail: gprasanta2008@gmail.com

INTRODUCTION

There is a need to study if domestic cats and dogs can be infected by Sars Co V-2 virus, and if so then whether the infected animals can also transmit the disease to human. The severe acute respiratory syndrome coronavirus (SARS CoV) was discovered[1] in 2002 in Guangdong province of southern China when the first infected human was identified. The virus was scientifically identified in 2003 in China. The virus SARS CoV is thought to be an animal virus. The animal reservoir is yet not confirmed but is thought to be the bats, which infect other animals such as the wild civet cats. Domestic animals have not yet identified to be its reservoir. The severe acute respiratory syndrome coronavirus 2 (SARS CoV2) causing COVID-19 flu was reported for the first time from China[2] during December 2019, through Dr. Li Wenliang, a medical doctor (and a whistleblower), who was working in a Wuhan hospital and who sent a message through "WeChat" to his friend about the disease. The chronology of events of the epidemic was being suppressed initially by the Chinese government. On January 11, 2020, on the Wuhan Health Commission public bulletin, it was disclosed that they had identified, "41 confirmed cases of coronavirus and one death. No

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new cases discovered since January 3, 2020." Later, on January 20, 2020, in a state television interview with Dr. Zhong Nanshan, a top coronavirus specialist of China, it was disclosed about the disease that "There's a clear proof for human-to-human transmission in Wuhan."

The complete nucleotide sequence of the genome of SARS CoV2 with 29,875 nucleotides was disclosed by China[3] on January 17, 2020. The present SARS CoV2 virus is, however, a mutated one, slightly different from the SARS CoV, and it infects only human; the spread is also from man to man.

The purpose of this article was to study if the tuberculosis disease burden of countries had any relationship with the present SARS CoV2 virus infection and mortality caused by COVID-19 disease.

METHOD OF STUDY

The published data on the web pages from the reliable sources were analyzed and conclusions were drawn from them.

ANALYSIS: The number of COVID-19 coronavirus-infected[4] individuals globally as of April 16, 2020, was 2,119,300. A total of 141,945 deaths were reported. Countrywide data were available from reliable web pages. They had been calculated from the aforementioned published figures that in developed countries the infected as well as the deaths were much more when compared to the corresponding figures reported from the developing countries [Table 1].

It can be seen from Table 1 that in terms of numbers as well as on the basis of percentage, the COVID-19 flu–infected individuals in countries such as the United States, Spain, Italy, and France were more (vide data in Columns 2, 3, and 4). In Brazil also, they were on the higher side. In China, India, Bangladesh, and Pakistan, they were comparatively lower. Comparison of data in Columns (2) and (5), infected per one million population and death per one million population, also shows that in the developed world, the more numbers were infected and more numbers died also.

It is also revealed that in developing countries such as Brazil, China, India, Bangladesh, and Pakistan, the number of infected as well as the number of deaths per one million population was way behind the corresponding figures observed for the developed nations. One reason for this can be that the numbers of confirmed infected individuals as well as the number of deaths from COVID-19 were underreported. But there can be other factors and reasons also.

The author is of the belief that where COVID-19 infections have taken place, there was a considerable negative relationship between the numbers of infected COVID-19 and their exposure to tuberculosis in the region. In other words, the more was the tuberculosis disease in countries, the less was the numbers infected with COVID-19.

The World Health Organization (WHO) has stated that it does not believe[6] that bacille Calmette–Guérin (BCG) vaccination protects people against the infection with COVID-19 virus. The global burden of tuberculosis as per the report[7] of the WHO (2019) is that per 100,000 populations, while Africa has a burden of 231, southeast Asia that includes India has a burden of 220. Against these figures, the incidence of tuberculosis is only 28 in Europe and 29 in the Americas. Even in Brazil, the tuberculosis-infected individuals per 100,000 was 45, which was much lower than those in Africa and southeast Asia. This implied that there would be more COVID-19 infected and COVID-19 deaths in Brazil, which was also unfortunately observed.

The hypothesis of the author, therefore, is that tuberculosis-prone zones have less the number of COVID-19 infected and COVID-19 deaths.

Table 1: Developed countries versus developing countries, corona SARS CoV2 infected and deaths figures as of April 16, 2020, along with estimated population[5] within brackets

Serial no. (1)	Countries with corona-infected cases and (population 2020 estimated) (2)	Deaths (3)	% Deaths compared to those infected (4)	Infected and (death in numbers) per one million of population (5)
1.	USA = 645,575 (331,002,651)	28,623	4.4%	1,950.4 (86.47)
2.	Spain = 182,816 (46,754,778)	19,130	10.5%	3,910.1 (409.18)
3.	Italy = 165,155 (60,461,826)	21,645	13.1%	2,731.6 (357.99)
4.	France = 147,863 (65,273,511)	17,167	11.6%	2,265.3 (263.00)
5.	UK = 103,093 (67,886,011)	13,729	13.3%	1,518.6 (202.22)
6.	Brazil = 29,015 (212,559,417)	1,760	6.1%	136.5 (8.28)
7.	China = 82,341 (1,439,323,776)	3,342	4.1%	57.2 (2.32)
8.	India = 12,759 (1,380,004,385)	423	3.3%	9.2 (0.31)
9.	Bangladesh = 1,572 (164,689,383)	60	3.8%	9.6 (0.36)
10.	Pakistan = 6,919 (220,892,340)	128	1.8%	31.3 (0.58)

DISCUSSION

The SARS CoV2 also called human coronavirus 2019 (HCoV-19) is an emerging virus and much knowledge is not yet available on the properties of the virus. It is realized that the virus is highly infectious; the transmission is from man to man. There is no reported zoonotic pathway for the corona SARS CoV2.

Regarding the ability of the new virus to infect individuals in different countries having different disease prevalence and different social habits, it is being observed by the author that the number of cases from the highly populated regions (such as southeast Asia, the African countries, and certain South American countries) is much lower than those reported in the regions of the developed countries [Table 1]. The timely availability of testing kits in the regions of developing countries was a problem, and there have been reports of shortages of testing kits in some pockets[8] of India. Yet, when there were adequate testing kits, even then the number of infected cases did not increase in the regions of developing countries at rates found in the regions of developed countries such as Europe and the United States [Table 1].

The author had the opportunity of working during 2002–2007 with a nonpathogenic mycobacterial species known as *Mycobacterium indicus pranii* (*M. indicus pranii*),[9] which was earlier known as Mw. The work was carried out at Cadila Laboratories, Ahmedabad, India (Cadila). It was found that the formulation[10] of Cadila based on *M. indicus pranii*, when administered to mammals, resulted in p38 inhibition, and therefore the pathways regulated by p38 protein could be modulated or stopped. The inhibition was found to last for more than 28 days. During that time, it was observed that this mycobacterium species behaved like mitogens and caused lymphocytes to multiply (unpublished results). Further, it was observed by the author that the heat-killed Mw-formulated product as the saleable product by the name Cadi-05, produced and sold by Cadila,[11] when injected into humans had invariably caused lesions at the site of injection. By observing the lesions, the author assumed that there was a cytokine storm at the site of injection. The inflamed injection site took approximately 3–4 weeks to heal without requiring any medication. The lesions in many cases required to be covered with sterile bandages. From these properties of Mw formulation, it was assumed by the author that all mycobacterium species would have properties to enhance the proliferation of lymphocytes because of the cytokine storm. If this was right then regions where tuberculosis was rampant, there the healthy inhabitants would have a marginal additional capability of having more lymphocytes in their bloodstream, which would impart them with *increased innate immunity characteristics* because of which the inhabitants living in the tuberculosis-infected area would have lesser COVID-19 infection compared to those staying in regions not infested by *Mycobacterium tuberculosis*. In tuberculosis-infested areas, almost every healthy individual encounters the tuberculosis bacteria in one form or the other during their life, and the luckier ones remain disease free because of the inherent stronger immunity.

Use of human noninfecting agents such as live BCG vaccines, Mw formulation (heat-killed Bacillus), and other such agents may impart some innate immunity against the COVID-19 disease because of the reasons discussed previously, but these strengths may not be enough to effectively protect from COVID-19 disease caused by the coronavirus SARS CoV2.

The corona SARS CoV2 virus enters into the human body through the angiotensin-converting enzyme 2 (ACE2) receptor protein, which is found in multiple tissues[12] in the epithelia of the lungs and the small intestine. Therefore, the disease can infect people through nose as also through the mouth by swallowing materials infected with corona SARS CoV2. Maintaining social distancing with people in the infected area is therefore important. Equally important is to use a mask to protect the nose and mouth from inhaling infected droplets.

It is not easy to develop an effective vaccine against the virus as this ribonucleic acid (RNA) virus is thought to mutate too often within a host and changes its proteins that are generally targeted for capture by the clonal immunoglobulins in vaccine therapy. It is also not easy to produce adequate quantities of activated clonal $CD8_+$ T cells, another strategy in vaccination, to enable the activated lymphocytes to kill the virus-infected cells and to opsonize the virus along with the macrophages. It was revealed from the nucleotide sequence alignment studies of the genome of SARS CoV2 that there are possibilities of 93 mutations[13] over the entire genomes of the virus; in India, there are already concerns[14,15] about the possibility of mutation in the virus. It is believed that the virus was possibility a natural[16] isolate that mutated and traveled from animals to human.

Besides the strategy of developing a vaccine against the virus, other strategies would include the synthesis of chemical substances, namely the analogs of adenine (A), guanine (G), thymine (T), cytokine (C), and uracil (U), that might be useful to prevent the virus from multiplication by synthesizing defective viral messenger RNA. Along with this strategy, other objectives would be to deactivate certain

vital viral proteins during its multiplication, assembly, and budding out from the infected host cells. These strategies are time-consuming and require sizable sums to be used for many years before any new drugs evolve.

RECOMMENDATIONS AND CONCLUDING REMARKS

There is room for belief that the healthy inhabitants residing in mycobacterium-infested regions of the world have better immunogenic capabilities to prevent infection from COVID-19, when compared with other healthy people residing in non-mycobacterium-infested regions. More study needs to be done to confirm this.

It needs to be ascertained if the mycobacterium species in general promoted more cell division of the lymphocytes of the host species, healthy or infected. In the meantime, the author is of the view that there is no harm in promoting the use of BCG vaccination among the adults, especially the senior citizens under the supervision of competent medical people. The newborn are already receiving BCG vaccines in the most developing countries through their existing programs of immunization. The developed countries that do not recommend the use of BCG vaccines in their childhood immunization program may like to consider its utility in their program.

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