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Indian Journal of Medical Sciences

Viewpoint

Interspecies transmission of coronaviruses and immunization: An Indian perspective

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Received : 24 July 2020
Accepted : 25 September 2020
Published : 31 December 2020

DOI
10.25259/IJMS_191_2020

Quick Response Code:

ABSTRACT

The milder form of infection and higher rates of recovery witnessed among COVID-19 patients in India is indicative of the potential intervention of other "unconventional" biological mechanisms. The recently established similarity between beta-coronavirus strains in animals and humans led us to hypothesize that previous contact with infected dogs or cattle could shield humans from the circulating SARS-CoV-2 virus. We further believe that our hypothesis, if confirmed by further studies, could be used as a potential vaccine strategy.

Keywords: COVID-19, Vaccine, Coronavirus, Animal vaccine, Pandemic

INTRODUCTION

Modern transport converts the world into a global village, allowing the rapid spread of infectious diseases. The current COVID-19 pandemic has spread to over 210 countries around the globe, including India.[1]

The SARS-CoV-2, like any other respiratory virus, is transmitted from an infected person to a susceptible host, through droplets, and surface contact.[2] There are currently seven characterized coronavirus strains (229E, NL63, OC43, HKU1, SARS, MERS, and SARS-CoV-2) known to be infective to humans.[3] Out of these, four strains cause milder forms of infection, while three others, including SARS-CoV-2, cause severe illnesses.[3]

The confirmed SARS-CoV-2 cases and associated mortality has been on the rise globally. COVID-19 has been declared a public health emergency and has put all health organizations on high alert. The need for a reliable vaccine or antiviral drug cannot be understated. From our current understanding of the disease, it is clear that the seriousness of the illness across geographical regions is different. Surprisingly, it is the developed nations that are more severely affected than the under-developed and developing countries. It is our understanding that a more in-depth analysis of this contrast may help build newer and more reliable therapies.

THE INDIAN SCENARIO

India's coronavirus fatality rate (FR) has been remarkably low compared to most other countries. Reported global COVID-19-associated FR is pegged at 7–7.5%. In contrast, with an FR of

2.87%, India is one of the lowest in the world.[4] Despite being a developing country with a significantly large rural/suburban population that lacks essential healthcare resources and facilities, India's remarkably low FR indicates a likely intervention of other factors and "unconventional" biological mechanisms in shaping the nature of this pandemic.

Researchers speculate that the relatively low numbers of elderly individuals in the population, high ambient temperature and humidity, mandatory administration of the BCG vaccination to the public, and possible resistance to malaria may have contributed to the low FR.[1,5] Even in the past, India has displayed relatively low mortality rates to infectious diseases such as tuberculosis and malaria, and it is critical to acknowledge a plausible link to epigenetic immune factors and understand their role in infectious disease prevention and prognosis.[5]

CORONAVIRUSES: A STRUCTURAL AND FUNCTIONAL PERSPECTIVE

SARS-CoV-2 infects epithelial cells of the respiratory tract through receptor-mediated endocytosis facilitated by Spike-protein-mediated recognition of and attachment to the ACE-2 receptor on the cell membrane. A recent study reported remarkably high levels of sequence similarity of ACE2 between domestic animals and humans.[6] Another study revealed that the Bovine and Canine Respiratory Coronaviruses displayed high-sequence homology to the SARS-CoV-2 Spike protein.[2,7] These findings suggested that the viral particles are likely to interact with a wide array of host cells, facilitating potential inter-species transmission.

Canine coronavirus

A recent study at the University of Ottawa traced coronavirus sequence similarity across different species and hosts and suggested that stray dogs are a likely source of the novel coronavirus SARS-CoV-2.[8] According to the authors, in canids, exposure to and subsequent intestinal infection caused by other SARS-CoV-2 would have eventually led to transmission to humans. Sequential evolutionary mutagenesis may have then conferred this virus with the ability of evading the human ZAP-mediated immune response.[9] Behaviors in canids, such as licking the anal regions during mating and other circumstances, could facilitate viral transmission from digestive to respiratory tracts. Critical evaluation of SARS-like coronaviruses in dogs and understanding their route of transmissions is thus imperative in our fight against COVID-19.

The Indian stray dog population stands at a whooping 35 million.[10] According to a recent report, between 7.5% and 54.7% of stray dogs are likely to have been infected with the canine respiratory coronavirus (CCoV). An extrapolation of these results is likely to yield a higher percentage incidence of CCoV in India, given the large stray dog population in the country. We suggest that due consideration should be given to a possible protective effect of CCoV against SARS-CoV-2.

Bovine coronavirus (BCoV)

The BCoV is a widely distributed pathogen and causes enteric or respiratory infections among cattle, leading to substantial economic losses to the beef and dairy industry.[11]

A recent study revealed a new selection pattern, along with the Spike protein indicative of the adaptive evolution of BCoVs, suggesting a successful mechanism for BCoV to circulate among cattle and other ruminants without disappearance[12] continuously. In addition, evolutionary mutagenesis in BCoVs and its high sequence similarity to several SARS-CoV-2 epitopes (primarily S proteins) suggest plausible cattle-to-human transmission.[2] In India, the cattle population is nearly 150 million.[13] Given the relatively common incidence of BCoV among cattle, India, on account of its abundant livestock population, is likely to yield a high percentage incidence of BCoV, thereby increasing the likelihood of interspecies transmission. Therefore, a possible protective effect of bovine respiratory coronavirus against SARS-CoV-2 must also be contemplated.

The potential link between India's extensive stray dog and cattle population with the country's milder course of infection and lower mortality rates is yet to acquire scientific validation. We believe that further understanding the role played by bovine and canine populations in shaping the SARS-CoV-2 pandemic in India is worthwhile considering their everyday interaction and contact with the general population and the risk of an animal to human transmission through droplet nuclei.[2]

In accordance with conventional principles of therapeutic immunology, it is safe to speculate that repeated exposure to canine and BCoVs, triggers a sequential cascade of immune responses in the human body-mediated through antigen-recognition and memory (cell-mediated and humoral) formation that helps generate long-lasting immunity against beta-coronaviruses, including SARS-CoV-2.[14] This, in turn, leads to partial or basal immunization. This could serve as an explanation as to why the rural/suburban Indian population, who are in constant interaction with livestock, are relatively more immune to SARS-CoV-2 than their urban counterparts.

FUTURE DIRECTIONS

The above discussion sheds light on the potential of canine and BCoV strains as candidates for human-SARS-CoV-2 vaccines. We hypothesize that these coronavirus strains, on isolation from Indian stray dogs and cattle, when adequately

attenuated, can be trialed as potential vaccine candidates. The limiting factor in our proposed hypothesis is the assumption that sufficient SARS-CoV-2 viral titers are transmitted from patient to patient.[15] Studies on animal coronaviruses have revealed that successful transmission through direct contact depended on the presence of high viral titers in respiratory and salivary aerosols.[8] Thus, further investigations assessing the rates and modes of interspecies transmission of CCoV and BCoV to humans are required to better suit our current hypotheses.

CONCLUSION

Human–wildlife interactions affect individuals' livelihoods, attitudes, and tolerance. Animals continue to play a crucial role in governing the emergence, etiology, and evolution of human pandemics. Given their pivotal role as viral reservoirs, it is vital to thoroughly evaluate their potential in conferring preventive immunity in humans and considers their prospects as therapeutic agents and vaccine candidates.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest. The author, Ashish Gulia is the editor of this journal. He does not have any competing interest.

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How to cite this article: Rao V, Kannan S, Arakeri G, Subhash A, Batra HV, Kumar J, *et al*. Interspecies transmission of coronaviruses and immunization: An Indian perspective. Indian J Med Sci 2020;72(3):167-9.