SARS-CoV-2 infection: physiological and environmental gift factors at high altitude

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Abstract Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has emerged as a global pandemic. This viral disease primarily causes lung pneumonia and has a wide range of clinical manifestations. The severity of infection ranges from those who are asymptomatic or with mild symptoms which do not require hospital admission, to those who require ventilator support and eventually die, depending on immunity, age and other comorbidities existing with the patients. The present report is an attempt to study the effect of physiological and environmental factors existing at high altitudes (HA) with spread of SARS-CoV-2 infection. Analysis of existing data revealed that HA natives do possess certain physiological advantages such as (1) improved hypoxic ventilatory response, (2) higher concentration of oxygen carrying molecules, haemoglobin, (3) increased production of Vitamin D, due to intense solar radiation, (4) lower rates of comorbidities such as lung infections, obesity etc. and (5) most importantly reduced production of angiotensin converting enzyme 2, a carrier molecule for SARS-CoV-2 virus entry into the host cell; all of which can collectively account for improved tolerance to SARS-CoV-2 infection in HA natives. In addition, environmental factors at HA such as (6) dry and chilly winds, (7) low air density and (8) intense UV radiations may further inhibit viral growth and spread into the atmosphere. We thus conclude that, high altitude natives may posses physiological and environmental advantage over low landers in terms of reduced severity of SARS-CoV-2 infection and its limited spread. Graphic abstract Gift factors associated with COVID-19 spread at high altitude.

Keywords SARS-CoV-2 · High altitude · Hypoxic conditions · ACE2 · UV radiation

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Rapid spread of pathogenic SARS-Coronavirus 2 (SARS-CoV-2) in various countries has lead to a global health emergency. This outbreak of the COVID-19 pandemic has stimulated diverse research on various aspects of disease worldwide. Although this disease has spread in almost every country on the globe, its epidemiological data availability is limited.

Recently we came across a few interesting studies and reports on COVID-19 spread in high altitude (HA) regions such as Tibet, Bolivia and Ecuador [1]. The epidemiological data available so far, demonstrates that high altitude natives (those residing above 2500 m sea level), are lesser susceptible to severe form of SARS-CoV-2 infection compared to those living in low lands [1]. The better adaptability of high altitude natives against the attack of this deadly virus could be due to several genetic and physiological adaptations in these individuals or it could also be attributed to the environmental conditions existing at HA. In other words, such naturally occurring adaptation mechanism and environmental conditions are ‘gift’ factors for high altitude residents that may mitigate the infection and spread of COVID-19. The possible underlying genetic mechanism may include, down regulation of angiotensin-converting enzyme 2 (ACE2) due to hypoxic conditions at HA [1], since ACE2 is the key transmembrane protein which facilitates entry of SARS-CoV-2 virus into the host cell. While ACE2, a vasodilator acts as counter balance for its homologue ACE1, a potent vasoconstrictor, both these enzyme of renin angiotensin system (RAS pathway) are sensitive to change in oxygen concentrations [2]. Under hypoxic conditions, ACE1 is up-regulated whereas ACE2 is down-regulated by the action of transcriptional regulator, hypoxia inducible factor-1 (HIF-1) [3, 4]. Thus since the inhabitants of HA have chronic exposure to hypoxic environment, they may have reduced production of ACE2 in pulmonary epithelial cells, which could be a limiting factor for viral entry and penetration into host cells, making them less susceptible to SARS-CoV-2. Although the epicentre of COVID-19 outbreak was Wuhan, China, clinical characteristics and outcome of the patients in different parts of China were different. A study conducted on 67 SARS-CoV-2 infected. Tibetan patients living in the Qinghai-Tibetan plateau concluded that a significant number of these patients (36 out of 67) were asymptomatic, and COVID-19 infection was milder in this high altitude area. Also, no deaths were reported from this study group [5].

The high altitude inhabitants are protected from wide range of tropical diseases, such as various dermatological conditions, parasitic and fungal infections due to its cold and dry environment. Climatic conditions at HA are also favourable to treat many pathological conditions like asthma, coronary artery disease (CAD), obesity and also gives improved longevity [6]. Low landers who travel to HA display various physiological changes in order to acclimatize to the acute severe hypoxia. The physiological attempt to maximize oxygen delivery under low oxygen requires extra energy expenditure, and thus they have increased basal metabolic rate [7]. However, in contrast to low landers both Andean and Tibetan highlanders display normal basal metabolic rate implying that their functional adaptations do not require increased basal oxygen requirements. They have better hypoxic ventilator response and maximal oxygen uptake under hypoxic environment and even higher concentration of haemoglobin for improved oxygen delivery compared to low landers, besides the fact that physiological routes of hypoxia adaptation amongst the two populations differ [8]. Since lungs are the prime target of SARS-CoV-2 attack, the improved lung capacity of HA inhabitants could act as a physiological boon against viral infection progression and the patient might experience a milder form of disease. In addition to this, thin, dry air and reduced pollen at HA is considered beneficial for several lung infections and contagious diseases [9]. Also HA environment facilitates increased synthesis of vitamin D due to strong solar radiations [10], which is advised as an important supplement for protection against COVID-19 infection [11]. Thus in conclusion, HA inhabitants have lower hazard ratio of other prevalent comorbidities associated with SARS-CoV-2, thereby providing an additional advantage of lower risk of severe infection and increased recovery rate.

Besides physiological adaptations of inhabitants, there are several environmental factors at HA which may also negatively impact virus spread. Extremes cold temperatures, wide difference between the day and night temperatures, dry and chilly winds, low air density due to low barometric pressure and intense ultra violet (UV) radiations are amongst the prime stressors which can potentially contain virus longevity and further spread. UV radiations have been proven to be an effective tool to kill wide variety of pathogens [12]. These UV radiations are very strong at high altitudes, above 3000 m and tend to increase further with altitude [13]. These might be critically important as UV-A and UV-B radiations are capable of altering genetic material like DNA and RNA [14]. SARS-CoV-2 virus settles on various surfaces and remain alive for several hours or days. The solar ultraviolet radiations may not only shorten half life of virus but also act as natural disinfectant to control community spread of virus at HA.

Keeping the said physiological and environmental factors in mind, we conclude that, virulence of SARS-CoV-2 might be less in high altitude areas with reduced severity of infection in HA inhabitants. Although very few clinical
reports are available so far which provide data on SARS-CoV-2 spread in HA population, more authentic data and studies in this regard, are required to substantiate these observations.

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