

Review Article

The Effect of Different Types of Climates on the Spread of COVID-19

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Abstract

Coronavirus disease of 2019 (COVID-19) is the third most common zoonotic disease caused by the coronavirus virus, SARS in 2002, and Middle East Respiratory Syndrome (MERS) in 2012. The primary origin of transmission of infection to humans is not well known. However, more prevalence of the disease is caused due to human-to-human transmission. There are relatively few studies on the impact of climate change on COVID-19 disease in the world. Recognizing the behavioral features of the SARS-CoV-2 virus and its pathogenicity in various climatic conditions can offer strategies for control measures, preventing the transmission of the disease, and minimizing the potential mortality risk of the virus, which provides a basis for more detailed studies in different climatic regions. This study aimed to evaluate the effect of different types of climate on the spread of COVID-19.

Keywords: Coronavirus disease of 2019 (COVID-19), Climate, Epidemiology

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Introduction

In late 2019, an acute respiratory disease with symptoms of pneumonia of unknown origin was found in Wuhan, China. Studies have shown this disease is caused by a new coronavirus, acute respiratory syndrome (SARS)-CoV-2 that quickly spreads from the sick person to the healthy person through respiratory droplet transmission. The disease spread through several cities in China and other countries, and following the epidemic on January 30, 2020, the World Health Organization (WHO) announced a state of international emergency then; in addition, this organization named the new

coronavirus disease COVID-19 on February 12, 2020¹. Gradually, the disease spread to most parts of the world, and WHO announced the COVID-19 outbreak as a pandemic on March 12, 2020.

COVID-19 is the third most common zoonotic disease caused by the coronavirus virus, SARS in 2002, and Middle East Respiratory Syndrome (MERS) in 2012. The primary origin of transmission of infection to humans is not well known. However, studies have shown that animals such as bats, anteaters, snakes, so forth are potential hosts for the virus. However, further studies are needed to determine whether the disease is transmitted directly from these animals or through intermediate hosts. Infection is likely to occur in the

seafood market for the first time. At present, the most important source of infection is patients and carriers^{2,3}. Coronavirus attributed infection can lead to lung damage and acute respiratory distress syndrome³, leading to lung disorders and death. Due to the rapid prevalence and spread of this disease, it can be concluded that the transmission power of SARS CoV-2 is higher than SARS-CoV. The disease is transmitted via various pathways, including person to person (direct contact) through respiratory droplets and indirect contact through fomites and aerosols⁴. Clinical manifestations of the disease include fever above 38.1°C, cough, fatigue and myalgia, shortness of breath, sore throat, and headache.

Moreover, digestive disorders such as diarrhea and vomiting have been reported in a small number of patients. The mortality rate is associated with the severity of the disease. According to the reports, the disease's incubation period lasts 1 to 14 days and, in most cases, between 3 and 7 days (1 and 4)⁴.

Coronaviridae is a large family of viruses genetically classified into four genera: alpha-coronavirus, beta-coronavirus, gamma-coronavirus, and delta-coronavirus that can cause diseases ranging from the common cold to more serious diseases such as SARS, MERS, and COVID-19². Among them, HCoV-NL63, HCoV-229E are belonging to alpha-coronaviruses whereas HCoV-HKU1, HCoV-OC43, SARS-CoV and MERS-CoV all of which belonged to beta-coronaviruses.

Human coronaviruses were first discovered in the mid-1960s in patients with the common cold, later called the coronavirus HCoV-229E and HCoV-OC43^{4,5}. Seven human-transmitted coronaviruses have been identified, such as SARS-CoV in 2003, HCoV NL63 in 2004, HKU1 in 2005, MERS-CoV in 2012, and SARS-CoV-2 in 2019⁶. The name "coronavirus" is derived from the Latin word corona or the Greek word κορώνη meaning crown or halo. This term is used to describe the appearance of virions (infectious forms of the virus), which under an electron microscope look like the crown of the sun or the royal crown⁷.

Coronaviruses are single-stranded, positive-sense RNA and belong to the order Nidovirales, family Coronaviridae. Their genome size ranges from ~26 to ~32 kb), one of the largest RNA viruses⁸.

Morphologically, coronaviruses are large spherical particles with an average diameter of about 120 nanometers. Their envelope diameter is about 80 nanometers, with spike lengths of 20 nanometers. Virus envelope is observed as a separate pair of dense electron shells in electronic micrographs consisting of a lipid bilayer containing membrane protein (M), envelope, and spike⁹. Virus glycoprotein not only is responsible for binding to the host cell but also contains the main antigenic epitopes, especially those epitopes that may fit to bind antibodies.

Furthermore, the virus glycoprotein plays a crucial role in binding and entry into the host cell, so targeting this protein with various drugs and inhibitory compounds is a strategy to fight Coronavirus or design a vaccine against this virus¹⁰. Some coronaviruses (specifically the members of Betacoronavirus subgroup A) comprise a shorter spike protein called hemagglutinin-esterase (HE)¹¹. Inside the viral envelope, there is a nucleocapsid composed of multiple copies of the nucleocapsid protein (N) binding to the positive single-stranded RNA genome. The envelope lipid layer, membrane proteins, and nucleocapsids protect the virus outside the host cell¹². At first, the most common cause of the illness was among travelers traveling to China or communicating with Chinese travelers. The disease is spread mainly through respiratory particles, and its symptoms are very similar to the flu, but due to the uncertainty about the transmission mechanisms of the new virus, all preventive measures are recommended¹³. Epidemiological research conducted in Wuhan demonstrated the initial link between the seafood market and most of the patients working there or going to these markets.

However, more prevalence of the disease is caused due to human-to-human transmission. Moreover, live rabbits, snakes, and other animals are sold in these markets¹⁴. On January 26, 2020, the National Health Commission of the People's Republic of China announced a total of 2,744 cases of pneumonia due to Ncov-2019 infection in 30 provinces, of which 461 were severe, 80 were fatal, and a total of 51 were treated and discharged. Currently, 5,794 suspected cases, 3,2799 close contact patients, and 3,0453 patients are still being tested. This is while the number

of patients in most countries, including Iran, increases daily¹⁴. According to epidemiological studies, the disease's incubation period is between 3 and 7 days to a maximum of 14 days¹⁵. Children and infants are also affected by Coronavirus 2019, but children's symptoms are relatively mild, and a small number of patients are in critical condition. More deaths have been reported in the elderly and people with chronic diseases¹⁶. Studies from December 16, 2019, to January 2, 2020, in Wuhan, China, have shown that the mean age of patients is 49 years, and chronic diseases such as diabetes, hypertension, and cardiovascular disease make the patient's condition worse¹⁷. Studies have shown that the clinical manifestations in patients with COVID-19 are similar to those of SARS-COV and MERS-COV infections, which may be due to similar pathogenic mechanisms. However, how this mechanism works in COVID-19 infection is not yet well understood. Some studies have shown that coronavirus respiratory infections occur primarily in the winter in temperate climates, although few cases have been reported occasionally in the fall or spring¹⁸. There are relatively few studies on the impact of climate change on COVID-19 disease in the world. Recognizing the behavioral features of the SARS-CoV-2 virus and its pathogenicity in various climatic conditions can offer strategies for control measures, preventing the transmission of the disease, and minimizing the potential mortality risk of the virus, which provides a basis for more detailed studies in different climatic regions.

2. Climate and infectious diseases

Different geographical regions of the world were classified into five climate-based, tropical, arid, temperate, Mediterranean, and polar¹⁹. The role of global climate change on human infectious diseases can be explored by its impacts on three characteristics of the disease: Pathogen, host, and environment. Humans are an important and active factor in this process. Climate change refers to long-term statistical changes in climate (change in average climatic conditions or moderate climate distribution). In addition, according to the European Environment Agency in the 20th century, since 1961, the global average temperature has increased by 0.74 degrees Celsius and the global sea level has been rising by

about 1.8 mm per year, and the Arctic sea ice has been decreasing by 2.7 per decade.

Furthermore, the mountain glaciers are shrinking, ocean waters are becoming more acidic, and most of the time, extreme weather events occur. Proper climatic conditions may affect infectious diseases by affecting pathogens, vectors, hosts, and living environments^{20,21}. Pathogens are defined as various infectious agents, including viruses, bacteria, parasites, and fungi. Climate change may affect pathogens either directly through influence on survival, reproduction, and life cycle of pathogens or indirectly through effects on habitat, environment, or other pathogens. In addition to geographical and seasonal distribution, the temperature is another important element influencing the life cycle and pathogenicity of pathogens owing to the requirement for a certain temperature to survive. In general, climatic conditions curb the geographical and seasonal distribution of infectious diseases, and the weather affects the time and severity of the outbreak. In studies, hot and unstable weather has a pivotal role in the global spread and redistribution of infectious diseases²². Many common infectious diseases, especially those transmitted by insects, are susceptible to climate change²³. The impact of climate change on several diseases, including vector-borne infectious diseases, including Deng, Malaria, Hantaviruses, and cholera, has been vividly observed²⁴. Prevalence of Salmonellosis²⁵ and giardiasis increase in rising temperatures and flooding conditions, unlike some diseases such as airborne diseases like influenza, and even others caused by food such as *Campylobacter*²⁶.

2.1. COVID-19 in tropical regions

Tropical regions are parts of the world near the equator, and in this zone, where the sun's rays reflect almost vertically, the climate is usually dry, humid, and rainy. In the northern hemisphere, the region is the distance from the tropic of Cancer to the equator, and in the southern hemisphere, it is located between the equator and the Tropic of Capricorn⁵. The WHO reports have shown that the disease can also occur in these areas, but statistics show that the disease's rate of spread and prevalence in the tropics is not as severe as in temperate regions^{7,12}.

In the following, we will examine the prevalence of the disease in some countries of the tropics.

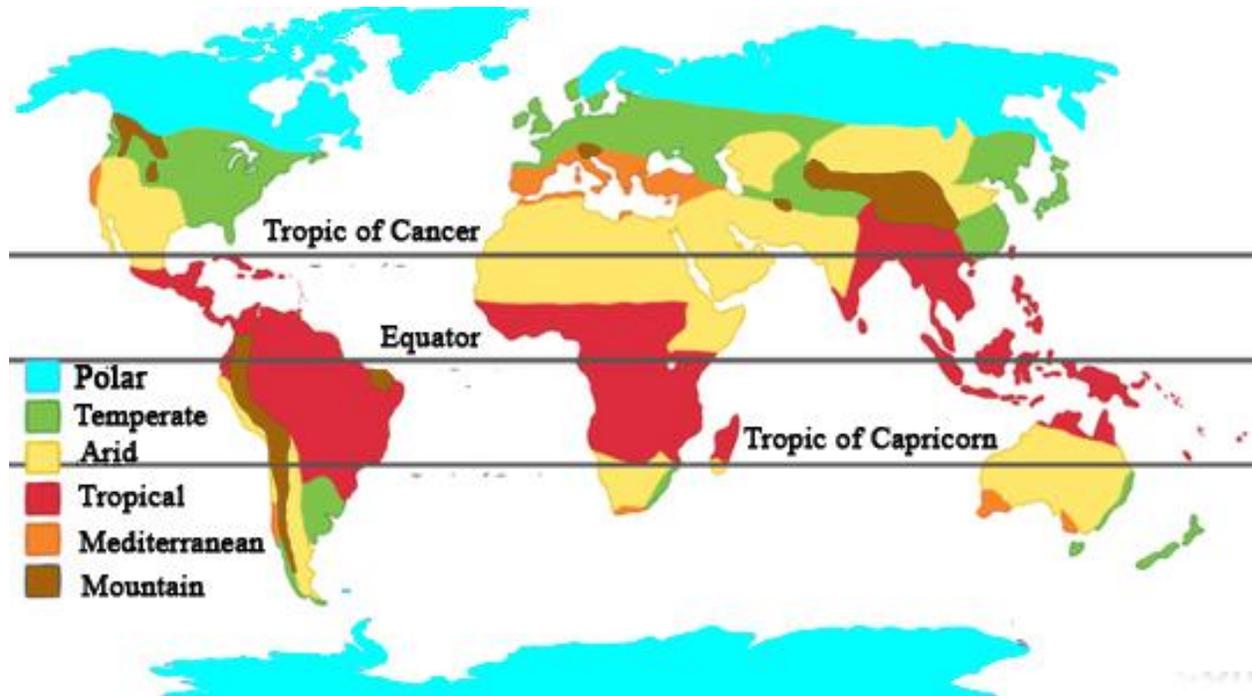


Figure 1. Classified geographical regions of the world based on different climates.

1) **India:** India is one of the areas most threatened by COVID-19 due to its location and geographical proximity to China as a source of disease and its large population. In other words, there are several risk factors in this country. However, the incidence of the disease has been lower than in countries such as Italy. WHO reports that as of October 28, 2021, the number of cases, improved cases, and deaths were 34,242,185, 33,615,182, and 457,165, respectively^{7,27}.

2) **Kenya:** Kenya is a country in East Africa. The first case of COVID-19 in this country was reported on March 13, 2020, in a 27-year-old woman traveling to London and the United States. Immediately upon identifying the first case, the Kenyan government identified the individuals who were in contact with the patient and quarantined them. As of October 28, 2021, WHO reports that the number of cases in the country is 253,018, of which 246,569 have recovered, and 5,270 have died²⁷.

3) **Somalia:** Somalia is a country in the Horn of Africa located in East Africa. According to the Ministry of Health of Somalia, the first case of COVID-19, a Somali citizen who had recently returned from China, was confirmed on March 16,

2020. According to the WHO report, as of October 28, 2021, there were 21,269 cases, of which 9,927 were cured, and 1,180 died²⁷.

4) **Brazil:** is the largest and most populous country in South America. Reports had demonstrated that some measures had been taken, such as quarantine and the separation of suspicious cases, before the cases were reported in the country. In addition, following the progression of the disease in this country, measures have been taken to prevent and reduce mortality. As of October 28, 2021, the WHO reports that 21,766,168 people have been infected. The rate of improvement and mortality was 20,965,296 and 606,726, respectively^{27,28}.

5) **Colombia:** is located in the northwestern part of South America. According to the WHO, as of October 28, 2021, there were 4,995,694 cases of the disease in the country, of which 4,839,391 were recovered, and 127,159 died²⁷.

6) **Indonesia:** is located in Southeast Asia and is generally considered the fourth most populous country globally. However, as of October 28, 2021, the reports of the WHO announced that the number of cases had been 4,242,532 people, of which 4,086,759 people recovered and 143,333 died⁷.

7) **Thailand:** One of the countries in Southeast Asia. The country has very fertile forest areas. As of October 28, 2021, according to the WHO, the number of cases of Covid19 in the country was 1,884,973, of which 1,766,823 improved and 19,006 died^{5,7}.

2.2. COVID-19 in desert / arid areas

Studies in China have shown that increasing the temperature by 1 degree Celsius leads to a 0.86 decrease in covid-19 disease. Studies have shown that the outbreak of COVID 19 is usually higher in dry and cold weather, while in extreme cold and heat conditions and humidity, its prevalence decreases. The fundamental mechanism of these climate change patterns is probably related to the virus's ability to survive in external environmental conditions before reaching the host. For instance, a recent study demonstrated that the survival of SARS-CoV-1 on surfaces at 11-25 degrees centigrade and relative humidity of 40-50 is more than five days³². Failure to tolerate high temperatures by coronaviruses is probably due to the lipid coating of the virus, which can be easily decomposed at high temperatures^{33,34}.

2.3. COVID-19 in temperate regions

The Northern Hemisphere's temperate regions are between the Arctic Circle and Tropic of Cancer, and the temperate regions of the Southern Hemisphere are between the Antarctic Circle and Tropic of Capricorn.

Currently, the highest incidence of the disease and the highest prevalence of the disease is in countries located in temperate regions—statistics and reports from the WHO have shown that coronavirus disease has spread rapidly in these areas. The following sentence shows statistics of some countries located in this geographical area²⁹.

1. **China:** The country is located in the temperate northern region and is the origin of the Corona 2 virus. In late 2019, acute respiratory illness with pneumonia of unknown origin symptoms spread to Wuhan, China. The disease spread to several cities in China and other countries, and following the epidemic, on January 30, 2020, the WHO¹ declared a state of international emergency, and then on February 12, 2020, the disease was caused by the new Coronavirus named COVID -19¹. According to the WHO, as of October 28, 2021, the total number

of cases in China is 96,938. The number of recovered cases is 91,643, and the number of deaths is 4,636 (5).

2. **Italy:** Italy is one of the most populous and touristic countries in southern Europe. During the recent pandemic due to the Coronavirus, this country experienced a horrible situation. As of October 28, 2021, According to the WHO, the number of cases is 4,757,231. There were also 4,548,449 deaths and 132,004 recovered cases^{5,7}.

3. **Spain:** The first case of Covid19 was reported in Spain on January 31, 2020. The first case was identified in Madrid on February 27, 2020. According to the WHO, as of October 28, 2021, the number of cases identified in Spain is 5,008,887. The number of recovered cases and deaths were 4,862,672 and 87,322, respectively^{7,9}.

4. **Iran:** The first confirmed case of the disease was reported by the Ministry of Health on February 19, 2020, in Qom. Iran's six neighbours, including Bahrain, Kuwait, Iraq, Oman, Afghanistan, and Pakistan, have reported that the first person returning to their country was a person who had returned from Iran. Furthermore, this revealed the pollution of Iran's airways. According to the WHO, as of October 28, 2021, the number of disease cases in Iran is 5,899,509, of which 5,468,620 were recovered, and 125,875 died.

5. **South Korea:** It is one of the countries in the temperate northern region that managed the spread of this virus, despite the widespread prevalence of the disease. Korea was one of the first countries to report cases of Coronavirus two outside China. The first case in the country was a 35-year-old Chinese woman who had travelled to Korea from Wuhan, China. According to the WHO, as of October 28, 2021, the total number of cases reported is 358,412, of which the number of recovered cases and deaths were 330,853 and 2,808, respectively^{57,11}.

6. **United States:** Most parts of the United States are located in temperate regions. It is one of the countries with the highest number of cases. According to the WHO, as of October 28, 2021, the total number of cases reported in the country is 46,601,658, and the number of recovered cases was 36,476,756, and the number of deaths was 761,954⁷.

7. **Turkey:** the first confirmed case of the disease was reported in Turkey On March 11, 2020. At present, as of October 28, 2021, the total number of cases is

7,936,007, of which the number of improved and mortality is 7,376,821 and 69,769, respectively.

2.4. COVID-19 in the Mediterranean region

Mediterranean climate is one of the climatic features of the Mediterranean region and is a type of semi-tropical climate. The lands around the Mediterranean Sea are the most significant region where this climate is found, and this Mediterranean climate is found in parts of the United States, California, in parts of western and southern Australia, in southwestern South Africa, in Central Asia, and parts of western and northern Iran, and central Chile. In the Mediterranean region, due to the type of subtropical climate, suitable temperature, and sufficient humidity, all of which provide suitable conditions for covid19 to survive outdoors, and the number of diseases in these countries is increasing³⁵.

2.5. COVID-19 in the Polar Regions Areas of the North and South Hemispheres adjacent to the North and South Polar Circuits: Countries in this region include Canada, Denmark, Norway, Sweden, Finland, Russia, and parts of the United States (Alaska)⁵. WHO reports have shown that the spread of the disease in Polar Regions is occurring at a slower rate^{7,12}. The latest statistics on these areas are given below.

1. **Canada:** The first case of Covid19 on January 27, 2020, was related to a man from Wuhan to Toronto. The Canadian government immediately took adequate measures to control the disease. As of October 28, 2021, the total number of cases reported in the country was 1,706,884, and 1,652,739 were improved, and the number of death was 28,881 (7).

2. **Russia:** Reports have indicated that as of October 28, 2021, the total number of cases of Covid19 in Russia was 8,392,697, and the number of recovered and deceased cases was 7,272,053 and 235,057, respectively⁷.

3. **Denmark:** According to the WHO, as of October 28, 2021, the number of disease cases in Denmark was 382,796, 364,002 people have improved, and 2,709 deaths have been reported⁷.

4. **Sweden:** As of October 28, 2021, the total number of cases reported was 1,170,422, 1,137,002 people were recovered, and the death toll was 14,984⁷.

5. **Finland:** As of October 28, 2021, the total number of cases announced was 156,959. The number of

recovered cases and the number of death cases were 46,000 and 1,150, respectively.

Discussion

Factors influencing the outcome of an infection that is key to the transmission and epidemiology of a disease are the ecology and behaviour of humans and the ecology and behaviour of the disease microbiome. Another factor to be mentioned is the immunity of the host and the host population. These variables interact with one another and are made up of a complex network of highly changeable characteristics. Moreover, the critical climate variables – temperature, rainfall, and humidity – cannot be viewed independently; the effects of temperature are modified by humidity, the daily range of each may be more significant than the daily mean, brief periods of atypical heat or cold can be more significant than long-term averages, heavy storms can have a different impact than prolonged light rainfall, one year's events may have a significant impact on subsequent years, and so on. In summary, any hypothesis on the impact of climatic factors must consider the complicated natural history of illness in the specific setting where it is transmitted³⁰. Thus, a comprehensive understanding of the role of climate on the immune system will help us enhance epidemiological predictions and ameliorate vaccine updating.

However, the role of weather is not fully understood despite many Laboratory investigations of host vulnerability to environmental circumstances and mathematical modelling techniques being used to investigate the relationship between influenza morbidity or fatality and meteorological variables³¹. Epidemics occur predominantly during the winter months in temperate nations³²⁻³⁴, in tropical and subtropical countries generally during the rainy season³¹. According to research, climate may influence influenza dispersion (onset, duration, and size) by influencing individual contact rates (frequency and duration), community immunity, and viral survival outside the human body. Temperature, humidity, rainfall, UV radiation, sunshine duration, and wind speed are all climatic factors that may influence influenza spread. Several laboratory works showed that cold and dry weather promotes a higher virus survival outside the human body and a better

transmission³¹. Cold air inhalation chills nasal epithelium, leading to an inhibition of the respiratory mucosa's mechanical defences and the immune system³⁵. There is a widely held belief that decreased vitamin D production throughout the winter reduces immunity and makes people more susceptible to seasonal infections in temperate areas. Some experiments show that a connection between vitamin D secretion and influenza protection^{36,37}. Because UV radiation is essential in vitamin D synthesis, a lack of UV radiation in winter decreases vitamin D production and increases influenza outbreaks in temperate regions^{38,39}. UV radiation and sunshine duration might indirectly affect influenza infections due to melatonin fluctuations' role in dark/light cycles and photoperiod on the immune systems⁴⁰. Finally, Xiao et al. (41) proposed that a low wind speed contributes to influenza spread in China. An intense wind speed may have a dispersive effect on influenza in the environment, limiting its diffusion.

Unlike many vitamins derived predominantly from food sources, vitamin D is produced endogenously in the skin upon exposure to sunlight. Ethnicity, skin pigmentation, socioeconomic status, geographic location, climate, and sunscreen; all of these factors contribute to the amount of insolation for any given individual. Low insolation creates the prerequisites for vitamin D deficiency. This is particularly true in HIV-infected individuals, highly vulnerable to vitamin D insufficiency/deficiency, as it plays a massive role in the musculoskeletal and cardiovascular systems. Antiretroviral therapy may also be a factor in vitamin D deficiency. Today, as the issues of preventing common skeletal and non-skeletal diseases with HIV-infected people are becoming highly relevant, maintaining vitamin D levels through exposure to sunlight or supplementation appears to be an effective and safe solution.

Vitamin D has a crucial regulatory effect on innate and adaptive immune responses. 1,25(OH)₂D₃ directly modulates the proliferation of T-lymphocytes, inhibits the development of Th17 cells, controls the differentiation of B cell precursors into plasma cells, prevents the production of Th1-associated cytokines and costimulatory molecules

(CD40, CD80, and CD86), and stimulates the production of Th2-associated cytokines. In particular, vitamin D supports antibacterial and antiviral immunity. In cases of vitamin D deficiency, the levels of proinflammatory cytokines increase, which significantly reduces the effectiveness of the immune response to infection⁴¹.

Chronic heat stress can negatively affect immune response in animals. Mice were infected with the H5N1 avian influenza virus as part of a study to see if CHS affected the mice's innate host immunity. CHS and thermally neutral groups of mice were used to experiment (TN). CHS therapy decreased local immunity in the respiratory tract, including the number of pulmonary alveolar macrophages and nasal mucosa, trachea, and lung lesions in the CHS group. Meanwhile, CHS slowed the development of dendritic cells (DCs) and substantially decreased IL-6 and IFN- γ mRNA levels. Mice were then inoculated with the H5N1 virus following the administration of CHS therapy. The mortality rate and viral load in the lungs of the CHS group were higher than those of the TN group. According to the findings, CHS therapy considerably suppressed local immunity in the respiratory tract and innate host immunity in mice and somewhat enhanced the pathogenicity of H5N1-infected animals⁴². These findings may also be accurate of COVID-19, which requires further research to prove.

According to another study performed on Nepalese children, it is implied that environmental conditions such as air pollution and cultural factors such as poor sanitation impact the overall health rate, particularly on children, because of their impotent immune system. Children under five years old are more prone to the ill effects of polluted environments because of their less well-developed immune systems. Around 12% of the population suffers from chronic respiratory diseases. In Nepalese hospitals, pneumonia is the leading cause of death for children under the age of five. Children are more prone to different infections for immunological, physiological, and social reasons. Their natural immunity declines within months after birth. The alveoli continue to increase throughout infancy, but the pulmonary reserve remains very limited⁴³. In another study, reasons for high seroprevalence of antibodies to varicella-zoster virus

in adult women in a tropical climate were explained for high mobility and immigration, leading to more communications in these regions inactivation of virus in humidity. Another description provided was "epidemiologic interference" with other prevalent viruses in a way that a high rate of disease transmission could lead to competition among different viruses for "soil," delay in natural transmission, and postponement of infection to adulthood. In this study, as reviewed above, the immune system was not mentioned to be a reason for too high seroprevalence of antibodies⁴⁴. The climate has a significant impact on VZV seroprevalence in Thailand. Warmer climates have a more significant delay in the establishment of natural immunity. Adolescent and adult susceptibility patterns were more prominent in rural than urban locations in the warmer regions, with population density as a secondary factor⁴⁵.

Consistently, many speculations on the potential impact of climate change on human health focus on malaria. Future climate changes may alter the prevalence and incidence of malaria, but the obsessive emphasis on "global warming" as a dominant parameter is indefensible; the principal determinants are linked to ecological and societal change, politics, and economics. In this study, an interconnected network of factors such as population immunity, vectors behaviour is implied to be effective³⁰. Also, influenza outbreaks are seasonal migration, rapid turnover within regions, and influenza strains that escape immunity and have the seasonal opportunity to establish and spread⁴⁶.

Another example is the specific microclimate of alpine waterfalls with high ionized water aerosols suggested to trigger beneficial immunological and psychological effects. The mucosal immune response analysis revealed a waterfall-specific beneficial effect with elevated IgA titers in the waterfall group⁴⁷.

Also, a study shows that some environmental properties such as high-altitude climate therapy are a well-established therapeutic option, which improves clinical symptoms in asthma. The study investigated the influence of high-altitude climate therapy on airway inflammation and cellular components of the specific and unspecific immune response. Exhaled

NO significantly decreased within three weeks of therapy in allergic and intrinsic, moderate, and severe asthma patients. Within three weeks of treatment, IL-10-secreting peripheral blood mononuclear cells (PBMC) increased in six out of 11 patients, whereas transforming growth factor-beta(1)-secreting PBMC remained steady in these patients. Monocyte activation, as measured by CD80 expression, also declined considerably throughout treatment. The frequency of CRTH2-expressing T cells decreased while regulatory T cells (T(reg)) remained stable. Eight out of ten patients had reduced interferon-gamma and IL-13 mRNA levels, but not FOXP3 or GATA-3 mRNA expression in CD4(+) T cells. High-altitude climate treatment, according to the most recent research, decreases inflammation in the airways. In addition, high-altitude climate treatment induces monocytes to adopt a tolerogenic phenotype. The T(reg)/Th2 ratio increases; however, because of the absence of antigens/allergens, no de novo differentiation of Th2 nor T(reg) cells are observed. Therefore, high-altitude climate therapy may form the immunological basis for the endogenous control of allergen-driven diseases⁴⁸. Consistently, profound changes in the immune system have been demonstrated at high altitudes, reducing B- and T-helper cell activation. Total and mite-specific immunoglobulin E antibodies decrease significantly during more extended sojourns. These changes are associated with reducing airway inflammation (e. g., reducing eosinophil activation, NO exhalation, and bronchial hyper-responsiveness). The fact that patients with non-allergic asthma demonstrate a reduction of their airway inflammation at high altitudes suggests that the high altitude climate has beneficial effects on asthma beyond the effects of allergen avoidance. High UV exposure and low humidity could be additional critical factors to explain the reductions in asthma severity in the high mountain climate⁴⁹.

It has been shown that Recreational winter exercise at moderately cold temperatures reduces allergic airway inflammation measured as FeNO, nasal eosinophilic cell count, and induces sustainable improvements in allergic symptoms⁵⁰.

Moreover, a study revealed higher human natural killer (NK) activity, increased anti-cancer proteins such as perforin, granzymes A and B, and granulysin

in natural killer (NK) cells, and lower stress hormone levels both men and women who visited forest parks but not cities. These results showed that going to a forest park once a month helped people retain more significant NK cells activity levels for almost 30 days following the excursions. The enhanced NK activity may be partly due to phytoncides produced by trees and a reduction in stress hormone production. A study found that going to forest parks increased the number of NK cells and their ability to release anti-cancer proteins, suggesting that going to forest parks may have a preventative effect on cancer development and progression⁵¹.

Temperature and rainfall are the primary climatic factors that have an impact on vector-borne disease ecosystems. Since vector bionomics is highly dependent on these factors, it affects many other systems, such as host behaviour and development and pathogen amplification. Several complicating factors are at play, making it difficult to determine how climate change may affect disease transmission patterns. As a result, a lot of what we know about these effects comes from mathematical models. Nevertheless, some direct evidence can be found for several vector-borne diseases. Evidence of the impact of climate change is available for malaria, arbovirus diseases such as dengue, and many other parasitic and viral diseases such as Rift Valley Fever, Japanese encephalitis, African human trypanosomiasis, and leishmaniasis. Temperature and rainfall variations and other severe occurrences were significant contributors to epidemics and are causing concern worldwide. Climate change quickly alters the geographic distribution of insect vectors, which is one of the primary driving factors.

According to research, heat stress weakens the immune system by affecting both cellular and humoral immune systems. Heat stress activates the HPA axis and raises glucocorticoid levels in the peripheral blood, suppressing cytokine synthesis and release. Heat stress has been shown to increase blood cortisol levels, which in turn inhibits the production of cytokines like interleukin-4 (IL-4), IL-5, IL-6, IL-12, interferon (IFN γ), and tumor necrosis factor-(TNF- α)⁵². It has been reported that heat stress impairs the cellular immune response by increasing the cortisol concentrations, which binds to DNA,

inhibiting the expression of genes involved in T-cell activation and cytokine production. The anti-inflammatory properties of corticosteroids result in a decrease in phagocytic cell activity and alter lymphocyte function. Heat stress influences the immune system by altering the Th1:Th2 ratio as the immune system attempts to maintain homeostasis; however, shifts from homeostasis may result in animals becoming immunocompromised and subsequently becoming more susceptible to diseases. Therefore, maintaining the Th1:Th2 balance could be a critical factor in minimizing the impact of immunological challenges during the summer season⁵².

There is an association between the month of vaccine administration and antibody responses to pertussis, PPV23, rabies, and *Salmonella* Typhi, vaccination, but there is no association between the month of vaccine administration and antibody responses to diphtheria, HepB, and tetanus, vaccination. African infants born in the wet season have more robust CD154 vaccine responses to BCG than infants born in the dry season. In adolescents, geometric mean antibody titers to HepB vaccination are lower in individuals who receive their first and second doses in summer than in those who receive them in winter. However, after the third dose, no statistically significant difference in geometric mean antibody titers is found. It has been suggested that these variations in vaccine responses may be explained through differences in exposure to ultraviolet (UV) irradiation. Nevertheless, exposing healthy volunteers to UV on five consecutive days before HepB vaccination does not lead to a difference in GMTs or cellular vaccine responses (in a lymphocyte stimulation test) between UV- and non-UV-exposed individuals⁵³.

UV light has been shown to reduce immunity⁵⁴. UV exposure may affect the immune response to vaccination or reinfection. UV exposure before and after infections significantly suppressed T-cell activity, leading to increased microbial load, increased severity of symptoms, and occasionally even death. If previously exposed to UV, humans may have more symptomatic infections at the risk of infectious diseases and would be less resistant to reinfections of these diseases⁵⁵. It is known that exposure of the skin to the UV wavelengths in sunlight stimulates systemic

immunosuppression, an outcome associated with reduced immunity to microbial infections in animal models. Studies show that the efficacy of vaccination can be reduced when surrogates of increased levels of sun exposure, such as latitude of residence and season of the year⁵⁶.

However, despite how complicated the process is, it is evident that molecules in the skin absorb UV light and alter their structure, which leads to immunological suppression. Significant roles are indicated for DNA and *trans*-urocanic acid (*trans*-UCA) as the initiators, the former becoming damaged and the latter isomerizing to *cis*-UCA. As a result of these changes, many molecules in the skin are produced, some called cytokines. As a result, they alter the functioning of two main T lymphocyte subsets that make up part of the white blood cell population in the skin and lymph nodes. T helper 1 cells, the first subset necessary to control tumor development, chemical reactions, and intracellular infections, such as those produced by viruses, are in a state of severe degeneration. In contrast, the second subset called T helper 2 lymphocytes, needed to control extracellular infections such as those caused by many bacteria, is not depressed to the same extent in the majority of systems analyzed thus far⁵⁷⁻⁵⁹.

Exposure of the skin to UV radiation results in:

1. Upregulation of innate immunity. Exposure of the skin to UV radiation results in the release of proinflammatory cytokines (signalling molecules regulating immunity), chemokines (molecules inducing directed chemotaxis), and antimicrobial peptides. The AMPs can be directly cytotoxic to pathogens and facilitate the cytotoxicity of natural killer cells and other cells of the innate immune system⁶⁰.

2. Suppression of adaptive immunity. Chromophores absorb UV photons in the skin. These include DNA, RNA, *trans*-urocanic acid (UCA), and membrane lipids, including 7-dehydrocholesterol, the precursor of vitamin D. Through a range of pathways, this results in upregulation of regulatory T (Treg) and B (Breg) cells and dampening of cell-mediated immune processes⁶⁰. Experimental studies show that sun exposure positively affects immune function and cardio-metabolic health, working through vitamin D and non-vitamin D pathways. From the effects of sun

exposure and vitamin D on immune function, these markers include DNA methylation of the FoxP3 gene to measure T regulatory cell number and function, total and house dust mite-specific IgE levels, varicella-zoster IgG⁶¹.

Studies have found that outdoor temperature and relative humidity are associated with global DNA methylation and gene-specific methylation in blood cells. It also found significant associations of air pollutants exposure with lower proportions of CD19+ B cell and NK cells⁶². There are still numerous unanswered concerns about the connection between air pollution and seasonal viral transmission. For example, high ozone levels, a well-studied pollutant, may cause lung inflammation. Rhinoviruses, it turns out, boost the immune system's response to ozone, resulting in higher amounts of the interleukin-8 (IL-8) hormone⁶³. Understanding the effects of environmental exposures on the human immune system requires investigating the relationship between air pollution and weather variables and blood leukocyte dispersion. The findings show that short-term air pollution exposure, temperature, and relative humidity are associated with leukocyte distribution⁶³.

The impact of climate change is also devastating because of the unpreparedness of Public Health Systems to provide an adequate response to the events, even when the climatic warning is available. However, evidence is robust at the regional and local levels. The studies on the impact of climate change on vector-borne diseases and health are producing contradictory results at the global level⁶⁴. New developing illnesses, climate change, microbe survival, and vectors are often connected. These diseases may exacerbate immune suppression caused by heat stress, controlled by the hypothalamus, pituitary, adrenal glands, and the sympathetic nervous system⁶⁵. Findings confirm that short-term ambient exposure to air pollutants, temperature, and relative humidity may be associated with subclinical but epidemiologically relevant inflammatory responses across the population.

Conclusion

In sum, increasing temperatures and prolonged sunlight exposure throughout summer may improve the impact of public health policies and initiatives to

restrict the spread of SARS-CoV-2. The risk of an epidemic resurgence, on the other hand, may rise throughout the winter. In addition, our findings imply that the disease would not be eliminated in the summer or near the equator without effective public health programs.

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Conflict of interest

The authors further declare that, they have no conflict of interest.

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