ISSN 2581-6217

World Journal of Pharmaceutical Science & Technology

Journal homepage: www.wjpst.com

Review Article

CORONAVIRUS DISEASE 2019(COVID-13): A LITERATURE REVIEW

Dr. Anita Yadav[1], Dr. Rekha[2], Dr. Priyanka [3]

1. Assistant Prof., Dept. of *Kayachikitsa*, SBMN Ayurvedic College, Rohtak, Haryana.
2. Assistant Prof., Dept. of *Prasuti Tantra Evum Stree Roga*, SBMN Ayurvedic College, Rohtak, Haryana.
3. Assistant Prof., Dept. of *Ayurveda Samhita & Sidhant*, Satya Ayurvedic medical college and hospital, Haryana.

Address for correspondence:

Dr. Ankita Yadav, Assistant Prof., Dept. of *Kayachikitsa*, SBMN Ayurvedic College, Rohtak, Haryana.
E-mail- dr.anitayadav89@gmail.com

Received: 15-12-2022, Revised: 29-12-2022, Accepted: 4-1-2023

ABSTRACT

In early December 2019, an outbreak of coronavirus disease 2019 (COVID-19), caused by a novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), occurred in Wuhan City, Hubei Province, China. On January 30, 2020 the World Health Organization declared the outbreak as a Public Health Emergency of International Concern. As of February 14, 2020, 49,053 laboratory-confirmed and 1,381 deaths have been reported globally. Perceived risk of acquiring disease has led many governments to institute a variety of control measures. We conducted a literature review of publicly available information to summarize knowledge about the pathogen and the current epidemic. In this literature review, the causative agent, pathogenesis and immune responses, epidemiology, diagnosis, treatment and management of the disease, control and preventions strategies are all reviewed.

KEYWORDS: COVID-19, Outbreak, SARS-CoV-2, Novel coronavirus

INTRODUCTION:

COVID-19 (**Coronavirus disease 2019**) is a contagious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The first known case was identified in Wuhan, China in December 2019[i]. The disease has since spread worldwide, leading to an ongoing pandemic[ii].

Symptoms of COVID-19 are variable, but often include fever, cough, headache, fatigue, breathing difficulties, and loss of smell and taste[iii]. Symptoms may begin one to fourteen days after exposure to the virus. Older people are at a higher risk of developing severe symptoms.

Transmission of COVID-19 occurs when people are exposed to virus-containing respiratory droplets and airborne particles exhaled by an infected person. People remain infectious for up to ten days after the onset of symptoms in moderate cases and up to twenty days in severe cases[iv].

In India, COVID-19 has 31216337 confirmed cases out of which 42015 are new cases and 418480 has confirmed deaths, this is the latest update of COVID -19 according to WHO on 21st July, 2021. This figure keeps changing every day.

Classical textbooks of Ayurveda describe *Jwara* as the most powerful among diseases capable of afflicting (to cause pain) body, mind and the senses[v]. Increase in temperature of body or mind is considered as the main feature of the disease[vi]. *Jwara* is a *Rasadhatu Pradoshaja Roga* affecting the *Abhyanthara Roga Marga* which includes the *Kostha* means *Aamashya*. *Rasadhatu Pradoshja Roga* is usually treated by *Langhana* and the same in various forms is used in the management of *Jwara* also.

This *Jwara* can also be classified as being *Agantuja* (external) caused by *Bhoota Abhishanga* (virus), which aggravates all the three *Doshas*. Considering the *Agantuja* and *Janapadodhwamsa* nature of the disease, COVID-19 can be considered as a type of *Sanipataja Jwara* / *Swashanaka Jwara* with high grade fever, tiredness, cough, breathlessness, aches and pains, nasal congestion, runny nose, sore throat, diarrhoea etc. as the main symptoms.

COVID-19 caused by the SARS-CoV-2 virus has already acquired an epidemic nature. Epidemics like COVID-19 are not new to Ayurveda and the classical textbooks have given a vivid description of such epidemics in the name of '*Janapadodhwamsa*'. Ayurveda clearly describes various aspects of such epidemics with respect to their cause (*Nidana*), effects, management and prevention. *C*haraka Samhita clearly explains that such epidemics manifest as a result of vitiation of air, water, environment and season which are common to all individuals. Hence such epidemics affect people irrespective of their physical constitution and the strength of affliction depends on the inherent *Dosha* vitiation of the person. *Prajnaparadha* (misuse of intellect), a causative factor for vitiation of all the *Dosha*, is considered to be the main cause of '*Janapadodhwamsa*'[vii]. Proper use of medicines to improve the physical health, judicial administration of five

elimination therapies and *Rasayana*, along with *Daivavyapasraya Chikitsa* has been mentioned as preventive and as treatment for diseases leading to *Janapadodhwamsa*.

The coronavirus pandemic has turned the world's attention to the immune system, the body's defense force against disease-causing bacteria, viruses and other organisms that we touch, ingest and inhale every day. The immune system plays a critical role in our response against infectious disease. Further, Poor mental health conditions, including stress and depression, are associated with increased risk of acute respiratory infections.

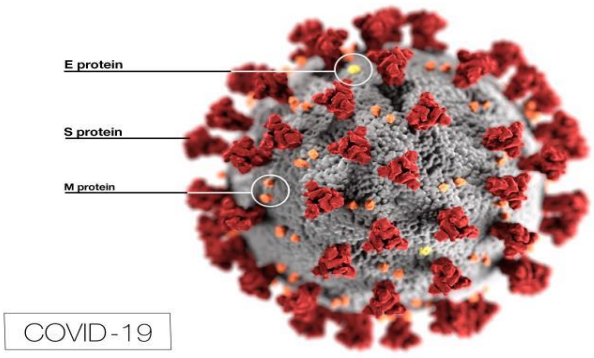
ETIOLOGY

Coronaviruses (CoVs) are positive-stranded RNA (ssRNA) viruses with a crown-like appearance under an electron microscope (*coronam* is the Latin term for crown) due to the presence of spike glycoproteins on the envelope. The subfamily *Orthocoronavirinae* of the *Coronaviridae* family (order *Nidovirales*) classifies into four genera of CoVs:

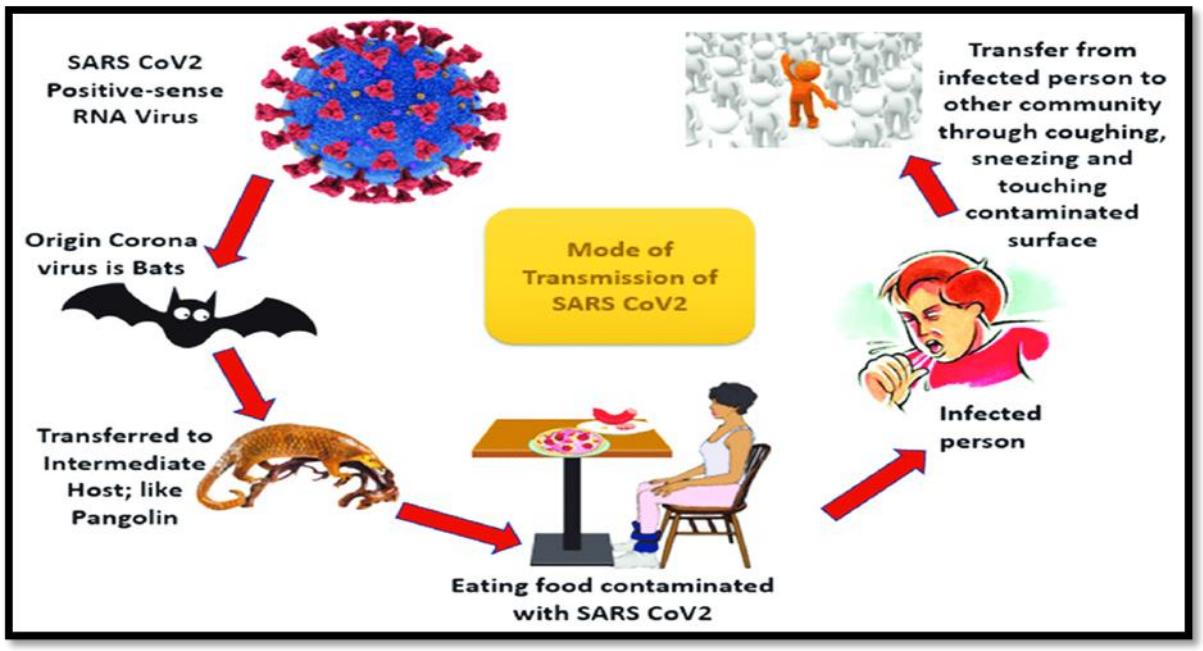
- **Alphacoronavirus** (alphaCoV)
- **Betacoronavirus** (betaCoV)
- **Deltacoronavirus** (deltaCoV)
- **Gammacoronavirus** (gammaCoV)

Common human CoVs: HCoV-OC43, and HCoV-HKU1 (betaCoVs of the A lineage); HCoV-229E, and HCoV-NL63 (alphaCoVs). These viruses can cause common colds and self-limiting upper respiratory tract infections in immunocompetent individuals. However, in immunocompromised subjects and the elderly, lower respiratory tract infections can occur due to these viruses.

Other human CoVs: SARS-CoV and MERS-CoV (betaCoVs of the B and C lineage, respectively). These viruses are considered to be more virulent and capable of causing epidemics manifesting with respiratory and extra-respiratory manifestations of variable clinical severity.

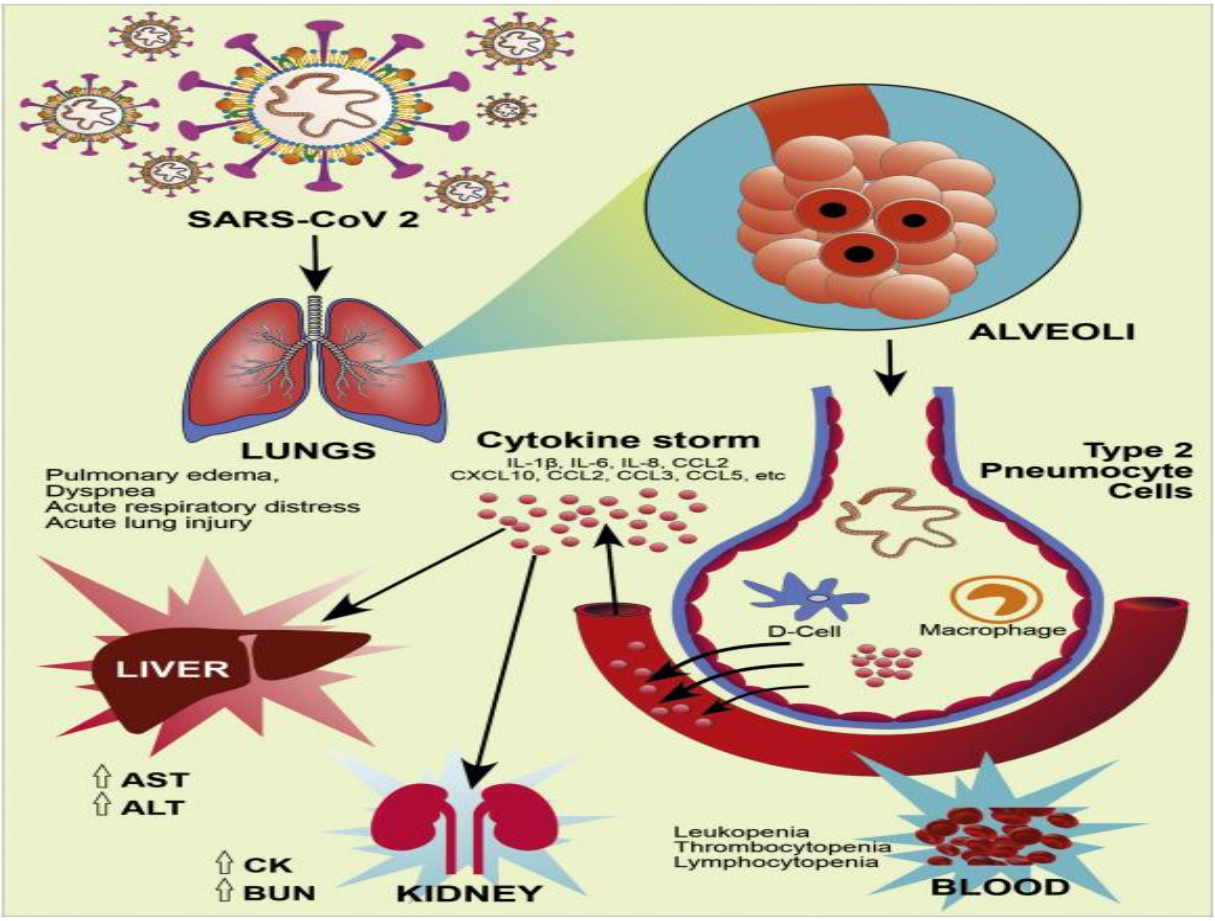


TRANSMISSION OF SARS-COV-2



- The primary mode of transmission of SARS-CoV-2 is via exposure to respiratory droplets carrying the infectious virus from close contact or droplet transmission from presymptomatic, asymptomatic, or symptomatic individuals harboring the virus.
- Airborne transmission with aerosol-generating procedures has also been implicated in the spread of COVID-19. However, data implicating airborne transmission of SARS-CoV-2 in the absence of aerosol-generating procedures are emerging and being evaluated. However, this mode of transmission has not been universally acknowledged.
- Fomite transmission from contamination of inanimate surfaces with SARS-CoV-2 has been well characterized based on many studies reporting the viability of SARS-CoV-2 on various porous and nonporous surfaces.
- Under experimental conditions, SARS-CoV-2 was noted to be stable on stainless steel and plastic surfaces compared to copper and cardboard surfaces, with the viable virus being detected up to 72 hours after inoculating the surfaces with the virus[viii].
- Viable virus was isolated for up to 28 days at 20 degrees C from nonporous surfaces such as glass, stainless steel. Conversely, recovery of SARS-CoV-2 on porous materials was reduced compared with nonporous surfaces.
- A study evaluating the duration of the viability of the virus on objects and surfaces showed that SARS-CoV-2 can be found on plastic and stainless steel for up to 2-3 days, cardboard for up to 1 day, copper

- for up to 4 hours. Moreover, it seems that contamination was higher in intensive care units (ICUs) than in general wards, and SARS-CoV-2 can be found on floors, computer mice, trash cans, and sickbed handrails as well as in the air up to 4 meters from patients implicating nosocomial transmission as well in addition to fomite transmission.
- The Centers for Disease Control and Prevention (CDC) recently released an update stating that individuals can be infected with SARS-CoV-2 via contact with surfaces contaminated by the virus, but the risk is low and is not the main route of transmission of this virus.
- Epidemiologic data from several case studies have reported that patients with SARS-CoV-2 infection have the live virus present in feces implying possible fecal-oral transmission.
- A meta-analysis that included 936 neonates from mothers with COVID-19 showed vertical transmission is possible but occurs in a minority of cases.



PATHOPYSIOLOGY

- Structurally and phylogenetically, SARS-CoV-2 is similar to SARS-CoV and MERS-CoV and is composed of four main structural proteins: spike (S), envelope (E) glycoprotein, nucleocapsid (N), membrane (M) protein, along with 16 nonstructural proteins, and 5-8 accessory proteins[ix]. The surface spike (S) glycoprotein, which resembles a crown, is located on the outer surface of the virion and

undergoes cleavage into an amino (N)-terminal S1 subunit, which facilitates the incorporation of the virus into the host cell and a carboxyl (C)-terminal S2 subunit containing a fusion peptide, a transmembrane domain, and cytoplasmic domain is responsible for virus-cell membrane fusion. The S1 subunit is further divided into a receptor-binding domain (RBD) and N-terminal domain (NTD), which facilitates viral entry into the host cell and serves as a potential target for neutralization in response to antisera or vaccines**.** The RBD is a fundamental peptide domain in the pathogenesis of infection as it represents a binding site for the human angiotensin-converting enzyme 2 (ACE2) receptors. Inhibition of the renin-angiotensin-aldosterone system (RAAS), as previously hypothesized, does not increase the risk of hospitalization for COVID-19 and severe disease.

- SARS-CoV-2 gains entry into the hosts' cells by binding the SARS-CoV-2 spike or S protein (S1) to the ACE2 receptors abundantly on respiratory epithelium such as type II alveolar epithelial cells. Besides the respiratory epithelium, ACE2 receptors are also expressed by other organs such as the upper esophagus, enterocytes from the ileum, myocardial cells, proximal tubular cells of the kidney, and urothelial cells of the bladder. The viral attachment process is followed by priming the spike protein S2 subunit by the host transmembrane serine protease 2 (TMPRSS2) that facilitates cell entry and subsequent viral replication endocytosis with the assembly of virions.
- In summary, the spike RBD allows the binding to the ACE2 receptor in the lungs and other tissues. The spike protein of an amino acid site (polybasic site) allows the functional processing of the same by the human enzyme furin (protease). This process enables the exposure of the fusion sequences and, therefore, the fusion of the viral and cell membranes, a necessary passage for the virus to enter the cell.

CLINICAL MANIFESTATIONS OF COVID-19

- The median incubation period for SARS-CoV-2 is estimated to be 5.1 days, and the majority of patients will develop symptoms within 11.5 days of infection.
- The clinical spectrum of COVID-19 varies from asymptomatic or paucisymptomatic forms to clinical illness characterized by acute respiratory failure requiring mechanical ventilation, septic shock, and multiple organ failure.
- It is estimated that 17.9% to 33.3% of infected patients will remain asymptomatic.
- Conversely, the vast majority of symptomatic patients commonly present with fever, cough, and shortness of breath and less commonly with a sore throat, anosmia, dysgeusia, anorexia, nausea, malaise, myalgias, and diarrhea. Stokes et al. reported that among 373,883 confirmed symptomatic COVID-19 cases in the US, 70% of them experienced fever, cough, shortness of breath, 36% reported myalgia, and 34% reported headache.

- A large meta-analysis evaluating clinicopathological characteristics of 8697 patients with COVID-19 in China reported laboratory abnormalities that included lymphopenia (47.6%), elevated C-reactive protein levels (65.9%), elevated cardiac enzymes (49.4%), and abnormal liver function tests (26.4%).[58] Other laboratory abnormalities included leukopenia (23.5%), elevated D-dimer (20.4%), elevated erythrocyte sedimentation rate (20.4%), leukocytosis (9.9%), elevated procalcitonin (16.7%), and abnormal renal function (10.9%).
- A meta-analysis of 212 published studies comprising of 281,461 individuals from 11 countries/regions reported that severe disease course was noted in about 23% with a mortality rate of about 6% in patients infected COVID-19.
- The elevated neutrophil-to-lymphocyte ratio (NLR), derived NLR ratio (d-NLR) [Neutrophil count divided by the result of WBC count minus neutrophil count], and the platelet-to-lymphocyte ratio is indicative of a cytokine-induced inflammatory storm.

Based on the severity of presenting illness that includes clinical symptoms, laboratory and radiographic abnormalities, hemodynamics, and organ function. The National Institutes of Health (NIH) issued guidelines that classify COVID-19 into five distinct types.

- **Asymptomatic or Presymptomatic Infection**: Individuals with positive SARS-CoV-2 test without any clinical symptoms consistent with COVID-19.
- **Mild illness**: Individuals who have any symptoms of COVID-19 such as fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhoea, anosmia, or dysgeusia but without shortness of breath or abnormal chest imaging
- **Moderate illness**: Individuals who have clinical symptoms or radiologic evidence of lower respiratory tract disease and who have oxygen saturation (SpO2) ≥ 94% on room air
- **Severe illness**: Individuals who have (SpO2) ≤ 94% on room air; a ratio of partial pressure of arterial oxygen to fraction of inspired oxygen, (PaO2/FiO2) <300 with marked tachypnoea with respiratory frequency >30 breaths/min or lung infiltrates >50%.
- **Critical illness**: Individuals who have acute respiratory failure, septic shock, and/or multiple organ dysfunction. Patients with severe COVID-19 illness may become critically ill with the development of acute respiratory distress syndrome (ARDS) which tends to occur approximately one week after the onset of symptoms.

DIAGNOSIS

Molecular Testing

The standard diagnostic mode of testing is testing a nasopharyngeal swab for SARS-CoV-2 nucleic acid using a real-time PCR assay. Commercial PCR assays have been validated by the US Food and Drug Administration (FDA) with emergency use authorizations (EUAs) for the qualitative detection of nucleic acid from SARS-CoV-2 from specimens obtained from nasopharyngeal swabs.

Serology Testing

An antibody test can evaluate for the presence of antibodies that occurs as a result of infection. Antibody tests play an important role in broad-based surveillance of COVID-19, and many commercial manufactured antibody testing kits are available to evaluate the presence of antibodies against SARS-CoV-2 are available.

Other Laboratory Assessment

Complete blood count (CBC), a comprehensive metabolic panel (CMP) that includes testing for renal and liver function, and a coagulation panel should be performed in all hospitalized patients.

Additional tests such as testing for inflammatory markers such as ESR, C-reactive protein (CRP), ferritin, lactate dehydrogenase, D-dimer, and procalcitonin.

Imaging Modalities

Considering this viral illness commonly manifests itself as pneumonia, radiological imaging has a fundamental role in the diagnostic process, management, and follow-up. Imaging studies may include chest x-ray, lung ultrasound, or chest computed tomography (CT).

Chest X-ray

- Standard radiographic examination (X-ray) of the chest has a low sensitivity in identifying early lung changes; it can be completely normal in the initial stages of the disease.
- In the more advanced stages of infection, the chest X-ray examination commonly shows bilateral multifocal alveolar opacities, which tend to confluence up to the complete opacity of the lung. Pleural effusion can also be demonstrated.

Chest Computed Tomography (CT)

Lung Ultrasound

Ultrasonographic examination of the lung allows evaluating the progression of the disease, from a focal interstitial pattern up to a "white lung" with evidence of sub pleural consolidations.

CONTROL AND PREVENTION STRATEGIES

- Disrupting the chain of transmission is considered key to stopping the spread of disease[x].
- Isolating the cases and contact tracing are key to limit the further spreading of the virus in clinics and hospitals.
- Should be placed in a separated, fully ventilated room and approximately 2 m away from other patients with convenient access to respiratory hygiene supplies[xi].
- Isolating the infected people and educating the public to recognize unusual symptoms such as chronic cough or shortness of breath is essential
- Setting up temperature check or scanning is mandatory at airport and border to identify the suspected cases.

CONCLUSION

The current COVID-19 pandemic is clearly an international public health problem. There have been rapid advances in what we know about the pathogen, how it infects cells and causes disease, and clinical characteristics of disease. Due to rapid transmission, countries around the world should increase attention into disease surveillance systems and scale up country readiness and response operations including establishing rapid response teams and improving the capacity of the national laboratory system.

REFERENCE:

[i] Page J, Hinshaw D, McKay B (26 February 2021). "In Hunt for Covid-19 Origin, Patient Zero Points to Second Wuhan Market – The man with the first confirmed infection of the new coronavirus told the WHO team that his parents had shopped there". *The Wall Street Journal*. Retrieved 27 February 2021.

[ii] Zimmer C (26 February 2021). "The Secret Life of a Coronavirus – An oily, 100-nanometer-wide bubble of genes has killed more than two million people and reshaped the world. Scientists don't quite know what to make of it". Retrieved 28 February 2021

[iii] Saniasiaya J, Islam MA (April 2021). "Prevalence of Olfactory Dysfunction in Coronavirus Disease 2019 (COVID-19): A Meta-analysis of 27,492 Patients". *The Laryngoscope*. **131** (4): 865–878. doi:10.1002/lary.29286. PMC 7753439. PMID 33219539.

[iv] *Clinical Questions about COVID-19: Questions and Answers* Centers for Disease Control and Prevention.

[v] Agnivesha, Charak Samhita, revised by Charaka and Dridhbala, With introduction by Vaidya- Samrata Sri Satya Narayana Sastri with elaborated vidyotini Hindi commentary written by Pandit kashinatha pandey & Dr. gaurakhnath churvedi Chowkhamba Bharati Academy, Gopal Mandir Lane, Varanasi -221 001, (India), reprint 2009. Chikitsa-Shtana 3/4, pg. 70.

[vi] Agnivesha, Charak Samhita, revised by Charaka and Dridhbala, With introduction by Vaidya- Samrata Sri Satya Narayana Sastri with elaborated vidyotini Hindi commentary written by Pandit kashinatha pandey & Dr. gaurakhnath churvedi Chowkhamba Bharati Academy, Gopal Mandir Lane, Varanasi -221 001, (India), reprint 2009. Chikitsa-Shtana 3/31, pg. 75.

[vii] Agnivesha, Charak Samhita, revised by Charaka and Dridhbala, With introduction by Vaidya- Samrata Sri Satya Narayana Sastri with elaborated vidyotini Hindi commentary written by Pandit kashinatha pandey & Dr. gaurakhnath churvedi Chowkhamba Bharati Academy, Gopal Mandir Lane, Varanasi -221 001, (India), reprint 2009. Viman-Shtana 3/20 pg. 573.

[viii] van Doremalen N, Bushmaker T, Morris DH, Holbrook MG, Gamble A, Williamson BN, Tamin A, Harcourt JL, Thornburg NJ, Gerber SI, Lloyd-Smith JO, de Wit E, Munster VJ. Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1. N Engl J Med. 2020 Apr 16;382(16):1564-1567. [PMC free article] [PubMed]

[ix] Jiang S, Hillyer C, Du L. Neutralizing Antibodies against SARS-CoV-2 and Other Human Coronaviruses: (Trends in Immunology 41, 355-359; 2020). Trends Immunol. 2020 Jun;41(6):545. [PMC free article] [PubMed]

[x] Chan J.F.W., Lau S.K.P., To K.K.W., Cheng V.C.C., Woo P.C.Y., Yuen K.-Y. Middle East respiratory syndrome coronavirus: another zoonotic betacoronavirus causing SARS-like disease. *Clin Microbiol Rev.* 2015;28(2):465–522. [PMC free article] [PubMed] [Google Scholar]

[xi] Centers for Diseases Control and Prevention . 2020. Coronavirus disease 2019 (COVID-19) [Google Scholar]