



A REVIEW TO UNDERSTAND THE AYURVEDIC APPROACH OF THE ETIOPATHOGENESIS OF COVID-19 PANDEMIC

Dr. Archana Singh*¹ and Dr. Ashutosh Dwivedi²

¹Assistant Professor, Dept. of Roga Evam Vikriti Vijnana, Govt. Ayurveda College Rewa.

²Assistant Professor, Dept. of Swasthviritta & Yoga, Govt. Ayurveda College Rewa.

Corresponding Author: Dr. Archana Singh

Assistant Professor, Dept. of Roga Evam Vikriti Vijnana, Govt. Ayurveda College Rewa.

Article Received on 17/09/2020

Article Revised on 07/10/2020

Article Accepted on 28/10/2020

ABSTRACT

COVID-19 has rapidly spread around the world and turned into the world's most crucial health problem. As the disease posing massive health, economic, environmental and social challenges to the entire human population, the whole world is paying their best efforts to combat this global problem. In the sequence of efforts to combat this newly emerging, unpredictable disease of respiratory system, it is important to understand the pathophysiology of the disease according to different fraternity. Here in this article, an effort has been made to understand the etiopathological aspect of Coronavirus Disease 2019 with the perspective of Ayurveda & contemporary medical science to facilitate the management of the pandemic by proper interventions of preventive measures and drug administration.

KEYWORDS: Ayurveda, COVID-19, SARS-CoV-2, Etiopathology.

INTRODUCTION

The Corona virus disease 2019 (COVID 19) has rapidly spread around the world and turned into the most crucial health problem of the era. In the last 20 years several viral diseases arises and some of them were recorded as epidemics for example SARS-CoV in 2002, H1N1 flu in 2009 and MERS-CoV in 2012.^[1] These infections remain restricted to the certain parts of the world. But the COVID-19 disease which came in existence in December 2019 in Wuhan City of China spread all over the world so rapidly and declared as a public health emergency of international concern on 30th January 2020. Due to its high risk to spread and its severity WHO characterized COVID-19 as a pandemic on March 11th 2020.^[2] As the disease creates massive health, economic, environmental and social challenges to the entire human population, the whole world is paying their best efforts to combat this global problem. The World Health Organization has also recommended inclusion of traditional medicine in its COVID-19 strategic preparedness and response plan.^[3] As efforts are under process to find the effective treatment against this pandemic, it is must to understand the disease and its etiopathogenesis according to principles of different medical fraternity. Here in this paper an attempt has been made to understand the disease COVID-19 with different perspective of Ayurveda.

COVID-19 As *Janpadodhwansha-Janya Vyadhi* (Pandemic aspect of disease)

COVID -19 was introduced as an outbreak, then identified as an epidemic and just within few months became the largest health concern of the world and declared as a pandemic by WHO. So before going through the Ayurvedic approach of pandemic; an outbreak, epidemic and pandemic should be understood.

An **outbreak** is when an illness happens in unexpected high numbers, may be limited in one area or extend more widely. An outbreak can last days or years. An epidemic is when an infectious disease spreads quickly to more people than experts would expect. Its unusual and unexpected occurrence usually affects a larger area than an outbreak. An epidemic occurring over a very wide area spreads across countries or continents is known as Pandemic. It affects more people and more fatal than an epidemic.^[4,5]

The World Health Organization (WHO) declared COVID-19 to be a pandemic when it became clear that the illness was severe and that it was spreading quickly over a wide area.^[6]

The WHO's pandemic alert system ranges from Phase 1 -a low risk disease to Phase 6 -a full pandemic, which is as following^[7]

Phase 1: A virus in animals has caused no known infections in humans.

Phase 2: An animal virus has caused infection in humans.

Phase 3: There are scattered cases or small clusters of disease in humans. If the illness is spreading from human to human, it's not broad enough to cause community-level outbreaks.

Phase 4: The disease is spreading from person to person with confirmed outbreaks at the community level.

Phase 5: The disease is spreading between humans in more than one country of one of the WHO regions.

Phase 6: At least one more country, in a different region from Phase 5, has community-level outbreaks.

In Ayurveda, a concept similar to the epidemic is described by *Acharya Charak* under a broad heading '*Janapadodhwamsa*'. The word '*Janapadodhwamsa*' comprises of two words *Janapada* that means large population & the second word *Updhwamsa* stands for destruction. Which means the disease is affecting & causing damage of a large number of people. *Acharya Charak* devotes the entire chapter for discussion on epidemics and points out how people with different *Prakriti*, *Sara* etc. can be affected in same time by the same disease due to the influence of common etiological factors like air, water, place and time, but does not list or describe specific epidemic diseases.^[8] In order to explain the etiological aspect behind the *Japadodhwamsa*, *Acharya Charaka Adharam* i.e. non virtuous act as the root cause, which can be correlated with the sinful acts practiced in recent time like anti-national elements indulging in terrorism, crime, deforestation, not following government rules, practice of improper or uncooked non vegetarian food etc. In *Bhela Samhitā* the condition of the pandemic is stated as *Janamara*,^[9] whereas *Acharya Shushrut* has also described the condition as *Maraka*,^[10] and counted *Kasa* (cough), *Shawas* (breathlessness), *Vamathu* (nausea), *Prtishyaya* (cold), *Shiroruja* (headache), and *Jwara* (fever) as the ailments seen during *maraka*.^[11] *Dalhana* also included *Gandh-agyana* (loss of smell sensations) and *Bhrama* (impaired cognitive functions) in his commentary on this phrase, which are commonly reported symptoms of Covid-19.^[12]

When compared with the recent pandemic of COVID-19, inhalation of droplets from an infected person by a healthy person, travelling of an infected patient from one place to another, seasonal changes allow more natural transmission of SARS-CoV-2 virus responsible for this disease. These factors can be compared with the factors responsible for '*Janapadodhwamsa*' i.e. vitiated *Vayu*(air), *Desha*(habitat) and *Kala* (seasons).^[13,14]

For the management of epidemics preventive measures described in Ayurveda are as Collection of potent medicinal drugs before the outbreak of an epidemic, avoid sinful acts & intellectual errors, use of *Pancha-Karma*, *Rasayana Chikitsa* to enhance the immunity and strength, truthfulness, compassion for living being, charity, generosity, worshipping god, codes of conduct,

practice of mantras & auspicious rituals help to prevent the disease.^[15,16]

COVID-19 as *Aupasargika* or *Sansargaja Roga*: (Infectious aspect of the disease): COVID-19 is a highly infectious and potentially fatal disease of respiratory tract caused by Severe Acute Respiratory Syndrome Corona Virus-2 (SARS-CoV-2, 2019-nCoV). The World Health Organization (WHO) declared coronavirus a pandemic due to widespread scale of the outbreak within few months of its origin. For the week ending 16 August the cumulative total to 21.2 million confirmed COVID-19 cases including 7,61,000 deaths has been reported by WHO.^[17] The United Nations said the coronavirus pandemic is the worst global crisis since World War II. In terms of the number of confirmed coronavirus cases, the US, Brazil, India, Russia and Peru are the five most-affected countries.^[18]

Transmission of SARS-CoV-2 can occur through direct, indirect, or close contact with infected people through infected secretions such as saliva and respiratory secretions or their respiratory droplets, which are expelled when an infected person coughs, sneezes, talks or sings. These respiratory droplets are relatively heavy, do not travel far and quickly settle down to the ground. People can catch COVID-19 if they breathe in these droplets from a person infected with the virus. (This is why it is important to stay at least 1 meter away from others.) These droplets can settle down on objects and surfaces around the person and people can become infected-by touching these objects or surfaces, then touching their eyes, nose or mouth.^[19]

In *Ayurveda* the concept of infectious or communicable disease can be compared with the *Aupasargika* or *Sansargaja Roga*, described proficiently by *Acharya Shushruta* in the context of *Kushtha Nidana*. He says by *gatrasansparshata* (physical contact), *nihsvashata* (expired air), *Saha bhojnata* (eating with others in same plate), *Sahashayyanachapi*(sharing a bed), *vastramalyanulepanata*(using clothes, garlands, and paste) infectious diseases spread from person to person.^[20]

These concepts are very much relevant with the COVID-19 as it is clear that the primary transmission of SARSCoV-2 is due to direct(through breathing of through respiratory droplets) or indirect (by touching the infected surfaces or objects) contact of the infected person.

COVID-19 as *Agantuja Vyadhi*: In *Ayurveda* diseases are grossly classified into two types on the basis of their etiological factors. The disease caused by the vitiation of internal factors of the body i.e. *Doshas*, *Dhatu*, *Mala*, *Agni* etc. are considered as *Nija Roga* and the disease caused by the external factors are known as *Agantuja Roga*.^[21] In the context of *Jvara*, *Agantuja roga* are further classified into four types and named as

Abhishangaja, *Abhighataja*, *Abhicharaja* and *Abhishapaja*.^[22] Out of these four types the *Abhishangaja* type stands for the infectious origin and also named as *bhutabhishangaja jvara*.^[23] *Acharya Cakrapani* clarifies that *bhuta* means *vishakrimi* or a virulent organism while *Vijayarakṣita*, the commentator of *Madhavanidana* stated that diseases caused by *Bhutopasarga* (invasion of *Bhutas* like *Viṣakrimi*) can be contagious and spreads from person to person.

Due to confirmed infectious and viral origin of COVID-19, and presence of fever as the most common symptom of the disease, at some points it can be considered as *Bhutabhishangaja Jvara*. In *Jvara Pratishedha Adhyaya*, *Acharya Shushruta* stated *Bhutabhishanga* as a reason of *Vishama -Jvara*.^[24]

As the *Abhishangaja* type of *vyadhi* stands for the infectious-origin of disease and as the fever is the most common reported symptom of COVID-19, it can also be considered as *Bhutabhishangaja jvara* which is due to *Tridosha* vitiation. So if we have a thought of comparing the disease with *sannipatika jvara* of *agantuja* type according to *Acharya Charaka* it can be considered as *vatakapha-ulvana*, *pitta-avara sannipatika jvara* due to resemblance of symptoms like fever, chills, cough, anorexia, thirst, burning sensation and aches etc.^[25]

Nidana Panchaka of COVID-19 (Pathophysiology of COVID-19): According to modern medical science COVID-19 is a highly infective viral disease which primarily affects the respiratory system of the patient. The causative virus of the disease SARS-CoV-2 belongs to the β -coronavirus family, and is partially related with the known SARS-CoV and MERS-CoV according to genome sequencing. Same as SARS-CoV, SARS-CoV-2 uses angiotensin-converting enzyme 2 (ACE2) as its main receptor, which is broadly expressed in vascular endothelium, respiratory epithelium, alveolar monocytes, and macrophages. SARS-CoV-2 is capable of active replication in the upper respiratory tissues, as demonstrated by successful live virus isolation from throat swabs and detection of viral subgenomic messenger RNA (sgRNA) in cells of upper respiratory tract. Later in the disease course, viral replication also involves the lower respiratory tract, and generates secondary viremia, followed by extensive attack against target organs that express ACE2, such as heart, kidney, gastrointestinal tract and vast distal vasculature. This process of viral spreading correlates with the clinical deterioration, mainly taking place around the second week following disease onset. However, it has been generally recognized that disease exaggeration till the late stage is not only attributed to direct viral damage, but also a consequence of immune-mediated injury induced by SARS-CoV-2. Of note, two distinctive features have been noticed in severe and critical patients with COVID-19, progressive increase of inflammation and an unusual trend of hyper-coagulation.

Immune-mediated inflammation plays an important role in the pathogenesis of COVID-19. The progression of COVID-19 was associated with a continuous decrease in lymphocyte count and significant elevation of neutrophils. Meanwhile, inflammatory markers were markedly elevated including C-reactive protein, ferritin, interleukin (IL)-6, IP-10, MCP1, MIP1A, and TNF α . Reduced lymphocyte count and elevated levels of ferritin, IL-6 and D-dimer were reported in various studies to be associated with increased mortality of COVID-19.^[26,27,28]

Nidana Panchaka stands for five diagnostic descriptors of disease is comprises of *Nidana* i.e. causative factors or etiological factors of the disease, *Purvarupa* i.e. prodromal symptoms of the disease, *Rupa* i.e. clinical features of the disease, *Upshaya* i.e. therapeutic response of the disease and *Samprapti* i.e. pathogenesis of the disease. An attempt is being made here to give a preliminary outline of the *Nidana Panchaka* of COVID-19.

1. Nidana (etiology): As the disease is identified as a communicable disease the most common mode of transmission is exposure to respiratory droplet (during talking, coughing, or sneezing) of infected person. Prolonged exposure to an infected person (being within 6 feet for at least 15 minutes) and briefer exposures to individuals who are symptomatic for example coughing or febrile are associated with higher risk for transmission, while brief exposures to asymptomatic contacts are less likely to result in transmission. Contact surface spread (touching a surface with virus on it) is another possible mode of transmission. Maternal COVID-19 is currently believed to be associated with low risk for vertical transmission.

Acharya Shushruta described above *Nidana* as *Aupsargika Nidana* as stated above, and classified as an *Agantuja nidana* in *Ayurveda*. The role of additional supportive factors which influences the clinical course and progression of the disease like weather, diet, lifestyle and other host related factors are not clear yet and need to be studied further.

2. Purvarupa (Prodromal symptoms) - Symptoms that do not give a clear indication of a *dosha* imbalance can be described as *Purvarupa*.^[29] The symptoms of COVID-19 infection appear after an incubation period of approximately 5.2 days.^[30] As Ayurvedic physicians did not have direct access to COVID-19 patients, it is not possible to document the prodromal symptoms of COVID-19. Since fever and cough is the most common symptom of COVID-19, presentation of symptoms without fever and symptoms arising before cough can also be considered as the prodromal symptoms of the disease. Patients, those remain asymptomatic during the whole duration of infection, shows absence of any prodromal symptoms. Overall symptoms like anorexia, tiredness, restlessness, throat discomfort, loss of

sensations of smell and taste can be included as the prodromal symptoms of the disease.

3. Rupa (Clinical Symptomatology): *Jvara*(Fever), *Kasa*(cough) and shortness of breath (*Swasha*) are the most commonly reported symptoms of the disease which points to *Vatakapha* dominance. Association of *Pitta* related symptoms and clinical course described

earlier indicate that COVID-19 is a type of *Sannipata Vyadhi* may be a type of *Jvara*. Depending upon the strength of immune response of patients and presence of risk factors, a wide range of variations can be seen in clinical presentations of COVID-19, so we can categorized these patients on the basis of severity of symptoms as following:

Classification of COVID-19 patients on the basis of clinical features.^[31]

Asymptomatic	RT-PCR Test Positive. Without any clinical symptoms and signs and the chest imaging is normal.
Mild	Symptoms of acute upper respiratory tract infection (fever, fatigue, myalgia, cough, sore throat, runny nose, sneezing) or digestive symptoms (nausea, vomiting, abdominal pain, diarrhea)
Moderate	Pneumonia (frequent fever, cough) with no obvious hypoxemia, chest CT with lesions.
Severe	Pneumonia with hypoxemia (SpO ₂ < 92%)
Critical	Acute respiratory distress syndrome (ARDS), may have shock, encephalopathy, myocardial injury, heart failure, coagulation dysfunction and acute kidney injury. Emergency warning signs for COVID-19 are given below that Seek emergency medical care immediately. ^[32] <ul style="list-style-type: none"> • Trouble breathing • Persistent pain or pressure in the chest • New confusion • Inability to wake or stay awake • Bluish lips or face

4. Upashaya (Therapeutic Response): Ayurvedic clinical studies need to be conducted to elicit the *upashayatmaka* (positive effect) or *anupashayatmaka* (negative effect) of various interventions in the form of medicines (*Aushadha*), diet (*Ahara*) and activities (*Vihara*) to confirm the provisional assessment of *dosha* imbalance and other Ayurvedic parameters.

5. Samprapti (Pathogenesis)^[33] As described earlier the disease is considered as *Agantuja – Bhutabhishangaja Vyadhi*, the clinical progress of disease begins following exposure to infection (*Bhutopsarga*). *Doshas start getting vitiated* following exposure to infection (*Bhuta* i.e. the virulent virus of the disease SARS-CoV-2) and starts affecting the *Pranavaha strotas* and *rasavaha strotasa* in preliminary stages manifests as cough (*Kasa*), dyspnea (*Swasha*) and fever (*Jvara*). This phase of infection can be compared with the phase of viral replication on vascular endothelium, respiratory epithelium, alveolar monocytes, and macrophages which further causes secondary viremia. The further pathogenesis of the disease depends on the immune response of the patient and presence or absence of risk factors. Patients with competent immune functions and without obvious risk factors such as old age, co-morbidities etc. may generate effective and adequate immune responses to suppress the virus in the first or second phase without immune over-reaction. In contrast, patients with depressed immune function may have a higher risk of failing the initial phase and becoming severely ill with higher mortality. Secondary viremia, followed by extensive attack against target organs that

express ACE2, such as heart, kidney, gastrointestinal tract and manifests as symptoms of critical stages can be compared with the progressive involvement of other *Strotas* as described by *Acharya Charaka*.

Talking about the types of *Samprapti* the COVID-19, the disease can be understood as single disease (*Sankhya Samprapti*), as till date there is no classification had been reported. However, further clinical studies may help us to sub-classify COVID-19 on the basis of variations in *dosha* imbalance. A dominance of *vata* and *kapha* accompanied by mild degree of *pitta* is seen in the clinical course of the disease for *Vikalpa Samprapti*, whereas it can be considered as independent disease (*Svatamtra Vyadhi*) for *Pradhanya Samprapti*. Even the disease is independent in origin but the presence of pre-existing co-morbidities can worsen the condition and this can be understood with the concept of *Vyadhi-sankara*. Sign and symptoms of critical cases such as pneumonia, ARDS, fatal cardiac events, stroke etc. can be compared with complication (*Upadrava*) of the disease. In terms of *Balasarprapti*, the severity of the disease is highly variable as some of the patients remain asymptomatic throughout the course of disease, while others are categorized in mild, moderate and severe cases. Patients with pre-existing co-morbidities are failing to survive. Further studies and clinical observations are needed to understand the role of extrinsic and intrinsic factors to understand the *Balasarprapti* and *Kala Samprapti* as the disease is new and relation between the manifestation of the symptoms in relation to diurnal and seasonal variation is still to be understood.

Shatkriyakala (Clinical course of the disease)^[34,35] The term *Kriyakala* refers to the recognition of the stage of a disease's progress i.e. stages of pathogenesis, which helps to determine appropriate measure to correct the imbalance in *Doshas* according to stage of disease. It is comprised of *Kriya* and *Kala*, where *Kriya* means the choice of treatment used to improve the disturbance in *Doshas*, and *Kala* refers to the stage of progress of a disease. So the meaning of *Shatkriyakala* is 6 stages of treatment, and the stages are *Sanchaya*, *Prakopa*, *Prasara*, *Sthanasamshraya*, *Vyaktavastha* and *Bhedavastha*.^[36] As the newly identified COVID-19 is not described in Ayurvedic literatures, an attempt is being made in this paper to sketch a rough outline of the *Shatkriyakala* to understand the various stages of the disease.

Stage of *Sanchaya*, *Prakopa* and *Prasara*: we have already discussed about the *Agantuja* aspect of the disease therefore the first three stages of *Shatakriyakala* i.e. the stage of *Sanchaya*, *Prakopa* and *Prasara* are difficult to distinguish in case of COVID-19. But the phase of incubation period of the disease can be tentatively compared with these three stages can tentatively correlate the incubation period of COVID-19 with this phase. Being the *Agantuja* phase of pathogenesis, *dosha* specific symptoms may not be seen. During incubation period of disease presence of non-specific symptoms in mild form can be seen, such as throat discomfort, loss of taste, loss of smell, abdominal discomfort in the form of diarrhea etc., or the patient may be asymptomatic during these stages.

Stage of *Sthanasamshraya* or *Purvaroop* (stage of prodromal symptoms of disease): In this stage the aggravated *dosha*, start to localize to any part of the body described as *kha vaigunya*: weak or pre-defective site in *samhitas*, and the process of interaction between *dosha* and *dushya* (tissues) begins known as stage of *dosha-dushya sammurchana*.^[37] In this stage all the prodromal symptoms of disease appears. This stage is not well demarcated in available clinical documentation of COVID-19, but as the fever and dry cough is the most common reported symptom of the disease, the prodromal symptoms of fever and cough can be seen during this phase whereas most of the patients remain asymptomatic.

Stage of *Vyakti* (Symptomatic stage of the disease): In this stage, clinical features are well manifested and one can easily identify the disease. In case of COVID-19, as described previously under the heading of *Roop*, these clinical features can be classified in the categories of mild, moderate & severe, while some positive patients also remain asymptomatic during the course of the disease.

Stage of *Bheda* (Stage of complications of disease): In this stage *doshaja* type of disease can be decided and the diseases became *chirakari* (chronic) or *asadhya*

(incurable). In case of COVID-19, it can be compared with the critical stage of patient characterized by severe pneumonia, ARDS and hypoxia. This stage of COVID-19 is associated with higher rate of mortality.

DISCUSSION

On the basis of review of classical Ayurvedic literature, COVID-19 can be considered as an *Upsargjanya Agantuja Vyadhi* as the causative factors of the disease are very much similar to the causative factors of *Upsargjanya- Samsargaja Vyadhi* described by *Acharya shushruta*. The viral infectivity of the disease can be considered as the *Bhutabhisanga* described in *Agantuja jvara*. As the *bhutabhisanga* causes vitiation of *tridosha* in further stage, it can be also considered as *Sannipatika Agantuja Vyadhi*.

Due to variability in clinical presentation of disease and fever and cough as the commonest reported symptoms; it can be understand as *Vata-kapha-pradhana Sannipataja Vyadhi* with *Pitaja anubandha*, which primarily affects the *Pranavaha & Rasavaha strotas*. On the basis of classical and modern review the pathological factors (*Samprapti Ghatak*) can be considered as following.

Samprapti Ghatak

Dosha- Tridoshaja Vatakapha Pradhan Pitta Anubandha.

Dushya - Rasa and other *Dhatus* in the later stages of the disease.

Vyadhi Swabhava – Ashukari, Atyayik(acute) .

Strotas- Rasavaha & Pranavaha Strotas in early stage and later on involvement of other *Strotas*.

Stroto Dushti Prakara - Vimarga Gamana, Sanga, Atipravritti.

Agni – Vishamagni.

Adhishthana- Pranavaha Strotas and later *Sarva Shareera.*

Vikara Prakriti – Daruna, Atyayik.

Sadhyatasadhyata - Sadhya in stages of *Sanchaya* and *Prakopa*, and *krichra sadhya* in stages of *Prasara* and *Sthana Samshraya*. *Asadhyaa* in the stage of *Bheda* especially in the cases of elderly persons with existing co-morbid factors and *Alpa Rogi Bala*.

CONCLUSION

COVID-19, the biggest health problem of the era is a new and erratic disease, which is not described in Ayurveda. So it can be considered as an *Anukta Vyadhi*, and to understand the disease and its pathogenesis the various Ayurvedic principles are reviewed and applied. An Ayurvedic assessment of the disease can help to classify the clinical presentations of COVID-19 on the basis of the *tridosha* framework and will be helpful to develop the treatment strategy.

On the basis of review of classical Ayurvedic literature, COVID-19 can be considered as an *Upsargjanya Agantuja Vyadhi* in the form of *Bhutabhisanga* and

having symptoms of *Vatakaphapradhana Sannipataja Vyadhi* with *Piitaja anubandha* primarily affecting the *Pranavaha & Rasavaha strotas*. Further clinical studies are desired to build a detailed description of the clinical course of COVID-19 from an Ayurvedic perspective. A proper understanding of disease will be helpful to form an effective Ayurvedic protocol for the management of disease which can be incorporated with allopathic protocol for a better integrated approach of prevention and management of the pandemic.

REFERENCES

1. Kumar, S. U., Kumar, D. T., Christopher, B. P., & Doss, C. The Rise and Impact of COVID-19 in India. *Frontiers in medicine*, 2020; 7: 250. <https://doi.org/10.3389/fmed.2020.00250>.
2. <https://www.pharmaceutical-technology.com/news/who-declares-covid-19-pandemic/>.
3. World Health Organization COVID-19 strategic preparedness and response plan operational planning guidelines to support country preparedness and response Google Scholar, 2020.
4. AH Suryakantha, "Community Medicine With Recent Advances", Published by JAYPEE Brothers Medical Publisher (P)Ltd. New Delhi, IIIrd Edition, Chapter, 19: 268.
5. K. Park, "Park's Textbook Of Preventive And Social Medicine" Published by M/s Banarasidas Bhanot, 25th Edition Print Feb, "Principles Of Epidemiology And Epidemiologic Methods", 2019; 3: 101.
6. <https://www.webmd.com/cold-and-flu/what-are-epidemics-pandemics-outbreaks#1>.
7. <https://www.webmd.com/cold-and-flu/what-are-epidemics-pandemics-outbreaks#1>.
8. Caraka Samhita, Vimana Sthan, Janapada-upadhvamsaniya vimanam, Chapter 3/6, Available from <http://niimh.nic.in/ebooks/ecaraka/?mod=read> (assessed on 19 October), 2020.
9. Maharshi Bhela, Bhela-Samhita, edited with hindi commentary by Shri Abhay Katyayan, Published by Chaukhamba Surbharti Prakashn, Varanasi, Print:2017, Adhyaya 13/8-9, Pp. 76.
10. Shushruta Samhita, Sutrasthan, Ritucharya Adhyaya 6/17, Available from <http://niimh.nic.in/ebooks/esushruta/?mod=read> (Assessed on 19 October), 2020.
11. Shushruta Samhita, Sutrasthan, Ritucharya Adhyaya 6/19, available on <http://niimh.nic.in/ebooks/esushruta/?mod=read> (assessed on 19 october), 2020.
12. Dalhana commentary on Shushruta Samhita, Sutrasthan, Ritucharya Adhyaya 6/19, available on <http://niimh.nic.in/ebooks/esushruta/?mod=read> (assessed on 19 october), 2020.
13. Seema Himmtrao Thakare et al., "Janapadodhwamsa in Ayurveda & its comparison with recent COVID-19 Pandemic" *Int. J. Res. Pharm. Sci.*, 2020; 11(1): 297-303.
14. Garg G. COVID-19 Pandemic: The Ayurvedic Perspective IJATM [Internet]. 2020Jun.8 [cited 2020 Oct. 18]; 2(2): Available from: <https://ijatm.org/index.php/ijatm/article/view/40>.
15. Caraka Samhita, Vimana Sthan, Janapada-upadhvamsaniya vimanam, Chapter 3/12-18, Available from <http://niimh.nic.in/ebooks/ecaraka/?mod=read> (Assessed on 19 October 2020).
16. Seema Himmtrao Thakare, & Prashil Prakashrao Jumade. Janapadodhwamsa in Ayurveda & its comparison with recent COVID-19 pandemic. *International Journal of Research in Pharmaceutical Sciences*, 2020; 11(SPL1): 297-303. <https://doi.org/10.26452/ijrps.v11iSPL1.2716>.
17. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200817-weekly-epi-update-1.pdf?sfvrsn=b6d49a76_4.
18. <https://www.hindustantimes.com/coronavirus/corona-virus-outbreak-globally-covid-19-pandemic-latest-updates/>.
19. Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ, Prescott HC. Pathophysiology, Transmission, Diagnosis, and Treatment of Coronavirus Disease 2019 (COVID-19): A Review. *JAMA*, 2020; 324(8): 782–793. doi:10.1001/jama.2020.12839.
20. Shushruta Samhita, Nidan Sthan, Kushtha Nidana Adhyaya 5/33-34, available on <http://niimh.nic.in/ebooks/esushruta/?mod=read> (assessed on 18th october2020).
21. Caraka Samhita, Sutra Sthan, Ashtodariya Adhyaya, Chapter 19/6, Available from <http://niimh.nic.in/ebooks/ecaraka/?mod=read> (Assessed on 19 October 2020).
22. Caraka Samhita, Chikitsa Sthan, Jvara Chikitsa 3/111, Available from <http://niimh.nic.in/ebooks/ecaraka/?mod=read> (Assessed on 19 October 2020).
23. Caraka Samhita, Chikitsa Sthan, Jvara Chikitsa 3/115, Available from <http://niimh.nic.in/ebooks/ecaraka/?mod=read> (Assessed on 19 October 2020).
24. Shushruta Samhita, Uttara Tantra, Jvaraprathishedhiya Adhyaya 39/68, available on <http://niimh.nic.in/ebooks/esushruta/?mod=read> (assessed on 18th october2020).
25. Caraka Samhita, Chikitsa Sthan, Jvara Chikitsa 3/92, Available from <http://niimh.nic.in/ebooks/ecaraka/?mod=read> (Assessed on 19 October 2020).
26. Yuki, K., Fujiogi, M., & Koutsogiannaki, S. COVID-19 pathophysiology: A review. *Clinical immunology (Orlando, Fla.)*, 215, 108427. <https://doi.org/10.1016/j.clim.2020.108427>, 2020.
27. Kermani E. K., Khalili H., Karimzadeh I., "Pathogenesis, clinical manifestations and complications of coronavirus disease (COVID-19)" *Future Medicine*; Published Online:27 Aug 2020<https://doi.org/10.2217/fmb-2020-0110>, 2019.
28. Jin, Y.; Yang, H.; Ji, W.; Wu, W.; Chen, S.; Zhang, W.; Duan, G. *Virology, Epidemiology, Pathogenesis, and Control of COVID-*

19. *Viruses*, 2020; 12: 372. Available on <https://www.mdpi.com/1999-4915/12/4/372#cite>.
29. Madhavakar, Madhava Nidana, with Madhukosha teeka, revised by Vijayarakshita and Kanthadatta, and Vidyotini Hindi commentary by Shri Sudarshana Shashtri, Revised & Edited by Ayurvedacharya Shri Yadunandana Upadhyaya, Published by Chaukhambha Prakashana.
30. Q. Li, X. Guan, P. Wu, X. Wang, L. Zhou, Y. Tong, *et al.* "Early transmission dynamics in wuhan, China, of novel coronavirus-infected pneumonia" *N. Engl. J. Med.*, 2020; 10.1056/NEJMoa2001316 Google Scholar.
31. Yuki, K., Fujiogi, M., & Koutsogiannaki, S. COVID-19 pathophysiology: A review. *Clinical immunology (Orlando, Fla.)*, 2020; 215: 108427. <https://doi.org/10.1016/j.clim.2020.108427>.
32. Available from <https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html>.
33. Puthiyedath R, Kataria S, Payyappallimana U, et al. Ayurvedic clinical profile of COVID-19 - A preliminary report [published online ahead of print, 2020 Jun 12]. *J Ayurveda Integr Med*, 2020; S0975-9476(20): 30039-5. doi:10.1016/j.jaim.2020.05.011.
34. Chauhan A, Semwal DK, Mishra SP, Semwal RB. Ayurvedic concept of Shatkriyakala: a traditional knowledge of cancer pathogenesis and therapy. *J Integr Med*, 2017; 15(2): 88-94. doi:10.1016/S2095-4964(17)60311-X.
35. Dr. Ravi Joshi, Dr. Vidya Rani Joshi; "SHATKRIYAKALA A CLINICAL APPROACH" *wjpmr*, 2019; 5(2): 125-128.
36. Shushrut Samhita, Sutra Sthan, Vrana- prashana Adhyaya chapter 21/36, Available on <http://niimh.nic.in/ebooks/esushruta/?mod=read> (assessed on 18th october2020).
37. Shushrut Samhita, Sutra Sthan, Vrana- Prashana Adhyaya chapter 21/33, Available on <http://niimh.nic.in/ebooks/esushruta/?mod=read> (assessed on 18th october2020).