Pathogenesis of COVID-19: A Review on Integrative Understanding through Ayurveda

Rashmi P Gurao1, UR Shekhar Namburi2, Shobhit Kumar3, Nakul V Khode4, Darshan M Mahulkar5

Abstract

COVID-19 is a new pandemic disease declared by the WHO as a global emergency and caused due to severe acute respiratory corona virus syndrome-2 (SARS-CoV-2). In India also, the grip of coronavirus is tightening day by day. The scientists worldwide are striving vigorously to ascertain the nuances in the etiology, spread, and pathogenesis of new COVID-19 disease and pragmatic utilization of this knowledge for the development of standard drugs as well as treatment protocols for its successful management. Ayurveda has laid emphasis on the Roga Parijñana in the context of Nidana Panchaka and Shatkiyakala in the management of any disease and it act as a beacon especially in the case of novel diseases that surface from time to time. The present review study is to formulate the pathogenesis of COVID-19 in the light of Ayurveda through an integrated approach. The COVID-19 pandemic is considered as one type of Janapadodhwamsa. In Ayurveda, the microbial infection can be elucidated in the terms of Bhuta, Rakshasa, Graha, etc., having idiosyncratic manifestations. The coronavirus can be contemplated as distinct type of Bhuta affecting Pranavaha Srotasa and causing Bhutabhishangaja Jwara, which is one type of Agantu Jwara. Later as the disease advances, it gets metamorphosized into Nija Vyadhi (endogenous form) exhibiting as different forms of Jwara depending on the extent of vitiation of Doshas along with extensive Pranavaha Srotodushhti Jvikaras. The factors involved in pathophysiology of any disease mainly Nidana (etiology), Dusha, Dushya (Dhatu, Srotasa), and Agni are reciprocally interlinked with severity and stage of disease. It is crucial to recognize extent of vitiation of each of these factors in order to determine customized diagnosis and management for the patients of COVID-19. The integrative approach plays a vital role in meticulous comprehension of COVID-19 in terms of Ayurveda to recognize each stage for specific management.

Keywords: Ayurveda, Bhuta, Bhutabhishangaja jwara, COVID-19, Janapadodhwamsa, Nidana Panchaka, Pranavaha Srotodushi Lakshana, Shatkiyakala.

Introduction

In recent times, viral diseases appear to be a major public health concern globally. The latest coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory corona virus syndrome-2 (SARS-CoV-2).1 The World Health Organization (WHO) declared the outbreak as a pandemic on March 11, 2020.2 COVID-19 has resulted in severe morbidity and mortality, which badly affected the global economy and caused loss to employment to millions of people. In India, COVID-19 disease is disseminating very rapidly and the total numbers of cases reported on June 30, 2020 are 566,840 (active cases: 215,125, cured/discharged cases: 33,4821, death cases: 16,893, and migrated case: 1).3

The COVID-19 is a newly emerged pandemic disease. Healthcare providers and scientists across the globe are putting all efforts to find out the exact course of disease, histopathology, and exploring various treatment including antiviral therapy, plasma therapy, vaccines, etc., for COVID-19 cases. However, these efforts are still unable to produce significant outcomes especially in the treatment of COVID-19. Ayurveda emphasizes that Roga Parijñana (knowledge of disease) is very much essential for diagnosis before treating the disease.4 It is very important to understand about the etiology to pathogenesis for effective prevention and successful management of the disease. Nidana Panchaka is one of the unique principles of Ayurveda and main tool for understanding pathogenesis and establishing diagnosis of the disease. Its five component includes Nidana (etiology), Purvarupa (prodromal features), Rupa (classical signs and symptoms), Upashaya-Anupashaya (relieving and aggravating factors), and Samprapti (disease manifestation).5 Thereby, history, complaints, and detailed examination of patient through Trividhi or Shadvidhi or Ashtavidhi or Dashavidhi Parikshas will make the path for proper diagnosis of disease. Further, another tool Shatkriyakala is used to assess the stagewise pathogenesis, respectively, at six levels of disease. This knowledge is useful to restrict the progression and appropriate planning of the judicious stagewise management of disease.

In contemporary science, the epidemiology, etiology, and pathogenesis along with histopathology of COVID-19 pandemic disease is described and some of these are yet to be established clearly. In Ayurveda, it is cited that newly emerged disease without prior description or nomenclature can be clinically understood through evaluation of the presenting complaints in terms of

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The pandemic COVID-19 disease can be understood in Ayurveda as *Janapadodhwamsa* (affecting many people at a time and destructing the community as well as health of the people in respective places). However, knowledge of pathogenesis of disease is very important for precise administration of various treatment modalities to control the pandemic. The pathogenesis of COVID-19 in terms of Ayurveda can be understood more appropriately with the integrative approach for better management to avert mortality as well as for controlling the present pandemic disease.

**OBJECTIVES**

- To establish the pathogenesis of COVID-19 in terms of Ayurveda
- To establish *Nidana Panchaka* for the diagnosis of COVID-19
- To establish manifestations of COVID-19 in terms of Ayurveda

**MATERIALS AND METHODS**

All the relevant literatures including classical Ayurvedic texts with their commentaries were explored for the concept of *Bhuta*, *Jwara*, *Janapadodhwamsa*, *Aupsargika Roga*, *Nidana Panchaka*, and *Shatkriyakala* to establish pathogenesis and manifestation of COVID-19 in terms of Ayurveda, and electronic database including Google scholar, PubMed, different government health agencies websites, and Google search were also explored to collect the relevant data by using the keywords: coronavirus disease, SARS-CoV-2, COVID-19, Ayurveda, *Janapadodhwamsa*, *Aupsargika Roga*, *Nidana Panchaka*, *Shatkriyakala*, traditional medicine, WHO, etc.

**OBSERVATIONS AND RESULTS**

**COVID-19 as per Contemporary Science**

The outbreak of COVID-19, caused by a novel SARS-CoV-2, occurred at Wuhan City, Hubei Province, China, in early December 2019. COVID-19 has been impacting worldwide affecting large number of people in approximately more than 200 countries and territories. As per the initial trends, the affected cases were predominantly elderly people and also no significant gender difference was observed. The total combined case fatality rate was 2.3%. SARS-CoV-2 is a member of the family *Coronaviridae* and order *Nidovirales*, and various study findings suggest that the original host of virus might be bats. Coronavirus are enveloped, positive-sense RNA genome of ∼30 kb. They are largely divided into four genera; α, β, γ, and δ based on their genomic structure. SARS-CoV, Middle East respiratory syndrome coronavirus (MERS-CoV), and SARS-CoV-2 are classified under β coronaviruses.

The virus particle has a diameter of 60–100 nm and appears round or oval. SARS-CoV-2 may get inactivated by ultraviolet or heat at 56°C for 30 minutes and is also sensitive to most disinfectants such as diethyl ether, 75% ethanol, chlorine, peracetic acid, and chloroform. It was observed that more stable and viable virus was detected up to 72 hours on plastic as well as stainless steel than on chloroform. It was observed that more stable and viable virus was such as diethyl ether, 75% ethanol, chlorine, peracetic acid, and (vii) release of virion from infected cells via exocytosis and infecting new cells.

In severe COVID-19 patients, the immunological studies showed lymphopenia, particularly the reduction in peripheral blood T cells. Further, studies also report that there is increased (storming) plasma concentrations of pro-inflammatory cytokines, including interleukin (IL)-6, IL-10, granulocyte-colony stimulating factor (G-CSF), macrophage chemoattractant protein 1 (MCP1), macrophage inflammatory protein (MIP)1α, and tumor necrosis factor (TNF)-α.

In severe COVID-19 disease thrombosis, pulmonary embolism and also elevated hypercoagulable profiles like d-dimer as well as fibrinogen levels were observed. Mostly it indicates significant endothelial injury, as endothelium plays a major role in thrombotic regulation.

The SARS-CoV-2 infection could be divided into three phases: viremia phase, acute phase (pneumonia phase), and severe or recovery phase. Patients with good immunity without morbid factors (old age, comorbidities, etc.) may suppress the virus in the first or second phase. There is higher risk of progression of disease into severe/critical phase in immune dysfunction patients.

The clinical features of COVID-19 patients may be classified as mentioned in the Table 1.

The COVID-19 patients’ provisional diagnosis can be done initially through clinical features. However, the confirmation is achieved by real-time quantitative polymerase chain reaction (RT-qPCR), CT chest scan, and immune reaction-based tests.

**COVID-19 Analogy in Ayurveda**

In Ayurveda, the COVID-19-like pandemics are considered as *Janapadodhwamsa* (Epidemic) and in other context the same was also referred as *Maraka* (fatal). The *Janapadodhwamsa Vikaras* are manifested mainly due to vitiation of *Vayu* (air), *Jala* (water), *Desha* (soil or state or continent) and *Kalaa* (time or climate). *Adharma* (unethical practices) is the fundamental etiological factor for *Janapadodhwamsa Vikara*. However the invasion of *Bhuta* (microorganism) also plays an important role in the pathology of these *Vikara/diseases*. A major aspect of *Janapadodhwamsa Vikara* is that such disease manifests in many people residing in a *Janapada*, with similar cardinal clinical features. The contaminated air due to presence of *Visha* (toxins/bacteria/viruses) may cause diseases like cough, breathlessness, vomiting, common cold, headache, and fever irrespective of *Desha* (geographical area), *Dosha*, and *Prakruti* (body constitution).
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In *Janapadodhwamsa*, death of large population might occur due to invasion of *Bhuta*. In modern literature, the term *Bhuta* means creature/devil/spirit with unknown entity. Acharyas have defined *Bhutas* as *Pishacha* (devil), *Devadi* (spirit), *Graha*; *Amanusha* (creature or organisms), etc. It can be linked with present concept of microbes (bacteria, viruses, and other microorganisms). These are considered as external causative factors for producing *Agantuja Vyadhi*. The association or contagion with microbes can be equated with *Bhutabhishanga* as specified by the Acharyas while describing the *Jwara Nidana*. Thus, microbial diseases in Ayurveda can be grouped under *Bhutabhishanga Jwara*. Further, it is emphasized that vitiation of all the three *Doshas* viz., *Vata*, *Pitta*, and *Kapha* occurs in *Bhutabhishanga Jwara* and the symptoms are explicit to the type of *Bhutabhishanga*. *Bhutabhishanga Jwara* is a type of *Agantu Jwara* (fever caused due to exogenous factors).

In Ayurveda, some of the infectious diseases are categorized as *Aupsargika Roga* and *Samsargaja Roga* (spreads from one human to another human) and may progress in to epidemic or pandemic diseases and results in *Janapadodhwamsa*. The mode of transmission of such *Samsargaja Roga* diseases includes physical contact, exhaled air, eating together or sharing food, sharing bed, clothes, ornaments, cosmetics, etc. The hypothesis of pathophysiology of infection of novel coronavirus from the Ayurvedic perspective can be explained by considering it as a *Bhutabhishanga Jwara*, which is *Samsargaja/Aupsargika* in nature. Therefore, COVID-19 disease can be equated with *Bhutabhishanga Jwara* having manifestations explicit to *Bhuta* (coronavirus). In progression of the disease, the *Bhutabhishanga* (viral infection of the body) vitiates the *Tridosha* and gets transformed into *Nija Vyadhi* with the features of *Pranavaha Srotodushthijanya Vyadhi* and different forms of *Jwara* (endogenous diseases).

The range of manifestations in the COVID-19 patients suggests that the degree of vitiation of *Tridosha* is variable owing to magnitude of infection or individual *Sharira Bala* (immunity) of patients.

The affinity toward *Pranavaha Srotasa* can be attributed to *Swabhava* (nature) of the *Bhuta* (coronavirus). The *Hridaya* (heart), *Mahasrotasa* (alimentary canal), and *Rasavahi Dhamani* are *Mulasthan* (root or origin) of *Pranavaha Srotasa*. In the recent literature, it has been cited that *Hridayo* includes whole area adjacent to heart/thoracic cavity that includes lungs.

This region is the seat of *Prana* and *Udana Vayu* (related to respiration), *Sadhaka Pitta* (facilitating cell biological functions), and *Avalambaka Kapha* (protection and maintenance of organs). The modus operandi of *Shwasa Chikitsa* is recommended for treatment of *Pranavaha Srotas* disorders. The *Shwasa Vyadhi* is *Pittasthana Samudbhava* (originating from seat of *Pitta*). Further, it has been elaborated that *Amarshaya* is *Pittasthana*.

*Amarshaya* is also seat of *Kledaka Kapha*, which is the crucial of all types of *Kapha* as it influences the status quo of other *Kaphasthana*, *Urah* (thoracic cavity) being one of them. Thus, it also plays an important part in pathology of *Pranavaha Srotas Vyadhi*. Manifestations related to gastrointestinal disturbances are also apparent in *Pranavaha Srotas Vyadhi*, *Mahasrotasa* (alimentary canal) being *Mulasthan* for *Pranavaha Srotas*.

*Amarshaya* is the common seat of *Kapha* and *Pitta Dosha*. Therefore, *Dushhti of Sthana* (abode) leads to *Pitta Dushhti*. The amalgamation of *Vikrut* *Kledaka Kapha* in *Amarshaya* also vitiates the *Prakrit Dushti*. *Vikrut* *Pitta Dushti* causing *Daha*, *Raga*, *Paka*, and *Shopha* (inflammation) in the body. Analogous symptoms may be observed when *Pranavaha Srotas* is affected by *Dushtha Rakta Dhatu*.

In mild stage of COVID-19 after incursion of virus in to the *Pranavaha Srotas*, *Shopha* (inflammation) might develop. The *Shopha* (inflammation) is the prior stage of *Vrana/Kshata* (injury). Therefore, it can be rationalized that the subsequent phase of *Shopha* of *Pranavaha Srotas* is the damage to this *Srotas*, which may be the initial process for pulmonary tissue injury (may be *Uraekshata*). *Uraekshata* is caused due to injury to the thoracic region and no prodromal symptoms (*Avyakta Lakshana*) are observed prior to full manifestation of disease. This can be correlated with the stage of COVID-19 where test is positive but patients are asymptomatic. *Jwara* (fever) may be observed in prior stages of *Shopha* or as a manifestation of *Rakta Dushti*. The symptoms of *Jwara* related to specific *Dosha* are not observed at this point as it is an *Agantu Jwara*.

*Vata Prakopa* along with *Pitta Dushhti* may cause *Kapha Udirana* (excess increase), thereby amplifying unctuous *Dosha* in head resulting in *Pratishyaya* (rinitis). *Kapha Prakopa* along with *Pitta Dushhti* cause *Srotorodha* (blockage of respiratory channels), thereby reversing the course of *Prana Vayu* resulting in *Kasa* (cough). It is typically in this stage, irregular breathing manifests due to preliminary vitiation of *Pranavaha Srotos Mulasthan*. The other symptoms like *Chhardi* (vomiting), *Avipaka* (indigestion), *Atisara* (diarrhea), and *Udarshoola* (pain in abdomen) are also exhibited due to involvement of *Mahasrotasa*. The *Mahasrotasa* mainly comprises of *Amarshaya* to *Pakwashaya*. The vitiated *Samana Vayu* circulating throughout *Amarshaya* and *Pakwashaya* produces gastrointestinal symptoms. The vitiation of *Dosha* is minimal in the occurrence of *Jwara*, *Pratishyaya*, and *Kasa*. At this stage, *Pranavaha Srotas Dushhti* symptoms are mild in nature and easy to treat. It is analogous with symptoms of acute upper respiratory tract infection in mild stage of COVID-19.

### Table 1: Stages and clinical features of COVID-19

<table>
<thead>
<tr>
<th>S. no</th>
<th>Stage</th>
<th>Clinical features</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Asymptomatic</td>
<td>COVID-19 positive without any clinical features</td>
</tr>
<tr>
<td>2</td>
<td>Mild</td>
<td>Acute upper respiratory tract infection symptoms with fever, fatigue, myalgia, cough, sore throat, runny nose, and sneezing. The patients may show symptoms like nausea, vomiting, abdominal pain, and diarrhea. Further, loss of smell (anosmia) or loss of taste (ageusia) preceding the onset of respiratory symptoms may also be observed.</td>
</tr>
<tr>
<td>3</td>
<td>Moderate</td>
<td>Pneumonia (frequent fever, cough) with no obvious hypoxemia and CT chest lesions.</td>
</tr>
<tr>
<td>4</td>
<td>Severe</td>
<td>Pneumonia with hypoxemia (SpO2 &lt; 92%).</td>
</tr>
<tr>
<td>5</td>
<td>Critical</td>
<td>Acute respiratory distress syndrome (ARDS), may have shock, encephalopathy, myocardial injury, heart failure, coagulation dysfunction, and acute kidney injury.</td>
</tr>
</tbody>
</table>

5 Critical Acute respiratory distress syndrome
4 Severe Pneumonia with hypoxemia (SpO2 < 92%)
2 Moderate Pneumonia without hypoxemia (SpO2 ≥ 92%)
1 Asymptomatic COVID-19 positive without any clinical features
Jwara is the disease originating in Amashaya. The vitiated Dosh onset reaching Amashaya obstructs the seat of Jatharagni, thereby producing Agnimandya and Sama Rasa Dhatu. The vitiated Dosh along with Sama Rasa Dhatu blocks the Rasavaha and Swedavaha Srotas, thereby pulling out Ushna from its abode and propagating it via Rasavahi Dhamani carrying Rasa Dhatu into the whole body consequently resulting in Jwara.41

The intermediate vitiation of Vata and Kapha with Pittanubandha causes Vata Kapajha Jwara. The symptoms of the disease would vary depending upon the Amsamsa Dosha Vikalpa but symptoms of Vata-Kapha involvement, such as rigidity, feeling of heaviness in head, rhinitis, cough, pain in small joints, drowsiness, heaviness, moderate fever, and excess sweating,32 would be seen commonly.

In the later stage of Shopha/Dushti of Pranavaha Srotas, the patient may develop Urakshat. It is characterized by cough with phlegm, hematemesis, chest pain, pain at the costal angels, and diminution of body tissues (Sapta Dhatu). This sequelae progress to deterioration in vigor, color, taste, digestion, myalgia, fever, depression, diarrhea, and hematuria. The phlegm is yellow/greyish in color, having bad odor, string like appearance, and mixed with blood.43

Rasavaha Srotasa and Pranavaha Srotas can vitiate each other as both Srotas share the same Multathana, Hridaya.21 The symptoms related to Pranavaha Srotodushti are evident in the diseases of Rasavaha Srotasa, viz., Hridroda.44 Hence, Rasavaha, Srotodushti further increases the Pranavaha Srotos Dushti, thus aggravating the symptoms.

In the case of Vata Kaphajha Jwara and Urakshata, the vitiation of Tridosha is moderate but may aggravate depending on the involvement of vitiation of other Srotas45 especially Rasavaha Srotasa. These may be parallel with symptoms of acute lower respiratory tract infection with moderate stage of COVID-19.

The substantial vitiation of all the three Dosh leads to Sannipata Jwara. In case of Sannipata Jwara, moreover, variable extent of permutation and combinations of Vata, Pitta, and Kapha Dushti manifest differently.46 The Pranavaha Srotasa Dushti may exacerbate into Shwasa Upadrava may be parallel to Pratamaka Shwasa. It may be associated with Jwara (fever) and Murcba (giddiness) due to auxiliary vitiation of Pitta with predominance of Vata and Kapha Dosh.37 It can be equated with the severe stage of COVID-19.

The vitiation of Jatharagni owing to Tridosha Prakopa in Sannipata Jwara impairs various Dhatwagni and thereby results in the formation of Vikru Dhatu.48 Formation of Vikru Dhatu precedes vitiation of corresponding Dhatu and its Srotasa,49 consequently developing complications related to varied Srotasa in the body.

The persistent Pranavaha Srotodushti along with comorbidities of other Srotas instigate considerable vitiation of Vata Dosh directly causing Urdhwashwasa (labored respiration with Cheyne Stokes breathing) and/or Chhinashwasa (stertorous breathing/failing respiration) wherein there is progressive collapse of respiratory function.50

The Sannipata Jwara may aggravate into the most dangerous form Sama Sannipata Jwara with extensive and homogeneous vitiation of all the three Dosh.51 It manifest as intermittent cold and warm sensation, body aches in the form of pain in bones, joint pain, headache, tinnitus, choking sensation in throat, varying degree of drowsiness, giddiness, stupor, delirium, cough, dyspnea, disorientation, the spu tus contains phlegm with blood, flaccidity, insomnia, dehydration, restlessness, chest pain, decreased or absence of urine output and stool, subcutaneous bleeding, or purpura with patient either groaning or mute.51 It resembles to critical stage of COVID-19 with multiorgan failure, which ultimately leads to death.

The pathogenesis of disease can be understood as described in Flowchart 1. Further, the parallel viewpoint of pathogenesis of COVID-19 with special reference to Nidana Panchaka and Shatkriyakala is explained in Table 2.

**Prognosis**

In Ayurveda, Janapadodhwamsa Vyadhis are Sudaruna (not having good prognosis) and therefore it is advised to treat population before manifestation of disease.52 Bhutabhisanga instigate Tridosha Prakopa (Sannipataja) and it is always Dushchikitya (difficult to alleviate).53 The prognosis of any disorder is not good in pregnant women, children, and elderly; therefore, any disease is Kricchrasadhya (difficult to treat) in these populations.54

The magnitude of Bhutabhisanga (coronavirus infection), variable degree of vitiation of the Tridosha (Tar-Tama Bhava), and individual Sharir Bala, which is downgraded in the presence of comorbidities and old age, further contributes to the poor prognosis of COVID-19.

However, in the absence of comorbidities of other Srotas, the prognosis in the mild stage of disease (both asymptomatic and symptomatic patients) can be considered as good. In moderate cases, manifestation of Vata Kapajha Jwara along with the initial stage of Urakshata may have fair prognosis since these are Kricchasadhya Vyadhi (difficult to treat). Prognosis is poor in severe cases if the symptoms of Urakshata develops completely.33 The development of Pratamaka Shwasa, which is a Yapya Vyadhi,55 and presence of comorbidities can exacerbate the situation into severe stage further worsening the prognosis. In critical cases the prognosis is very poor or irreversible as disease progresses in to Sannipata Jwara along with Sama Sannipata Jwara46 and associated with Urdhwashwasa and Chhinashwasa,25 which are Asadhya Vyadhi.

The Shatkriyakala is one of the unique principles in Ayurveda, which explains the chronology/timeline of disease formation and its knowledge is crucial for ascertaining the prognosis and treatment.53 In COVID-19, the prognosis of the disease can be assessed as per Shatkriyakala in Table 3.

**Prevention**

COVID-19 is a Bhutabhidhangaja Vyadhi leading to Janapadodhwamsa due to its characteristic Samargaja/Aupsargik nature. The main cause of Janapadodhwamsa is Adharma, which is associated with basic hygiene.15 Being Samargaja/Aupsargik Roja, it spreads through close contact and droplet infection. Hence, for the prevention of this disease, practice of basic hygiene and practice of social distancing in general can be beneficial.

The Sharira Bala is also an important factor for the development of disease.57 Therefore, the treatment principles for enhancing Sharira Bala can be used for the prevention of COVID-19.

**Management**

In Janapadodhwamsa, the standard protocol for management of the disease is performing Pancavidha Shodhanam, administration of Rasayana, and specific drug therapies.7 Further adopting Sadvritta (ethical code of conduct),58 wholesome food habits as
well as lifestyle, and administration of other supportive therapeutic measures, Dhupana, etc., will help in breaking the pathogenesis for managing the COVID-19 pandemic disease.

**Discussion**

COVID-19 is a new pandemic disease that has affected many countries of the world. The pathogenesis of the disease is gradually explored by the contemporary medical science. For treating any disease successfully, the pathogenesis of the same should be understood precisely by the physician.

In Ayurveda, emphasis is given on the accurate diagnosis and understanding the manifestation of a disease through the knowledge of its pathophysiology from Nidana to Samprapti before initiating the treatment for any disease. Accordingly the physician should also acquire knowledge of the associated branches of the sciences.

COVID-19 is a pandemic disease caused by virus SARS-CoV-2, which can be considered under Janapadodhwamsa. In Ayurveda, microbiology is not described in terms of viruses or bacteria, etc. However, the terms like Krimi, Rakshasa, Bhuta, etc., were cited in the etiology of corresponding diseases. In the context of...
Table 2: Pathogenesis according to Nidana Panchaka and Shatkriyakala

<table>
<thead>
<tr>
<th>S. no</th>
<th>Shatkriyakala</th>
<th>Nidana Panchaka</th>
<th>Pathogenesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Samchaya</td>
<td>Nidana</td>
<td>Samghattala pravritta, Aupsargika/Samsargaja, and Bhutabhishhangaja, a type of Agantuja Vayadi. In the early manifestation stage of disease, no involvement of Dosh in the development of disease. The Chaya, Prakopa, and Prasara of Dosa occurs subsequently. This stage is comparable with asymptomatic stage of COVID-19.</td>
</tr>
<tr>
<td>2</td>
<td>Prakopa</td>
<td>Pratyaksha</td>
<td>The infection of coronavirus in Pranavaha Srotasa can be compared with Sthanasamshraya Avastha where the vitiated Dosa (here Agantu Dosa—virus) incorporates with vulnerable Srotasa. This results in vitiation of all the three Dosa due to innate characteristic of Bhutabhishhangaja. In this stage, prodromal symptoms of disease occur with mild symptoms like Jwara, Pratishtayaa, and Kasa due to minimal vitiation of Doshas (mild stage of COVID-19).</td>
</tr>
<tr>
<td>3</td>
<td>Prasara</td>
<td>Purvarupa</td>
<td>Vata—Kapha Pradhanaa Pittanubandhi; Bhutabhishhangaja Jwara Laghu, Tiksha, Snigda, Tikta, Katu Rasatmaka, Ushna Virya Aahara Dravya, and Aushadhi Guru, Ruksha, Khara, Madhura, Amla, Kashaya Rasatmaka, Shita Virya Aahara Dravya, and Aushadhi. Further, there is need for conducting the clinical trials to confirm the provisional assessment as per the Doshas/stage of disease, etc. on basis of Upashaya and Anupashaya.</td>
</tr>
<tr>
<td>4</td>
<td>Sthanasamshraya</td>
<td>Janapadodhwamsa</td>
<td>It is the stage of chronicity and complications. The prognosis becomes poor in this stage. The Bheda stage of COVID-19 can be associated with Sama Sannipata Jwara, Urdhwashwasa, and Chhinndashwasa (severe and critical stage of COVID-19).</td>
</tr>
<tr>
<td>5</td>
<td>Vyakti</td>
<td>Rupa</td>
<td>Poor</td>
</tr>
<tr>
<td>6</td>
<td>Bheda</td>
<td></td>
<td>Poor</td>
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Table 3: COVID-19 symptoms according to Shatkriyakala with probable prognosis

<table>
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<tr>
<th>S. no</th>
<th>Shatkriyakala</th>
<th>COVID-19 symptoms</th>
<th>Prognosis</th>
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<tr>
<td>1</td>
<td>Sthanasamshraya</td>
<td>Asymptomatic, Jwara, Pratishayaa, Kasa</td>
<td>Good</td>
</tr>
<tr>
<td>2</td>
<td>Vyakti</td>
<td>Vata kapha Jwara, Urakshat, Pratamaka Shwasa Development of all symptoms of Urakshat, Sannipata Jwara.</td>
<td>Fair</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sannipata Jwara, Urdhwashwasa, Chhinndashwasa Comorbidities of other Srotasa in any stage</td>
<td>Poor</td>
</tr>
</tbody>
</table>

Janapadodhwamsa, it is described that the incursion of Bhuta may lead to mass destruction of population. Accordingly, SARS-CoV-2 virus can be understood as Bhuta.

Adharma (sinful acts) directly reflects about the stressful and awful psychological status of the individual and it is considered as one of the main causative factors in Janapadodhwamsa. The acute stress or chronic stress may affect components of the immune system. If this factor is analyzed, Adharma may be one of the main aggravating factors for gradual deteriorating in the immune system.

As per Ayurveda, the progression of disease depends upon status of three important factors including Nidana, Dosh, and Dushya and these factors are reciprocally interlinked with severity of disease. The status of Srotasa is also an important factor in pathogenesis of disease. After vitiation, Dosa get propagated in various Srotasa in Prasara Avastha. If Srotasa is in natural robust state, then there will be no further progression due to nonavailability of susceptible site for Sthanasamshraya of the vitiated Dosa and disease will not develop, whereas in case of comorbidities, the Srotasa is already vitiated by Dosa and have more susceptibility toward the disease owing to subsequent downgradation of the Sharia Bala. Therefore, more chances of development and rapid progression of disease in comorbid situations.

In the pathogenesis of COVID-19, after the entry of virus into the respiratory tract initially, virus spike protein engulfs with ACE2 receptors in the lungs, which may indicate vitiation of Vata and Kapha in mild and moderate stages of the disease.

In severe COVID-19 patients, lymphopenia, increased (storming) plasma concentrations of pro-inflammatory cytokines, including interleukin (IL)-6, IL-10, and tumor necrosis factor (TNF)-α, thrombosis, pulmonary embolism, and also elevated hypercoagulable profiles like d-dimer as well as fibrinogen levels, etc., are observed, which indicate extensive as well as homogeneous vitiation of all the three Dosa and subsequent vitiation of Rakta Dhatu.

In Ayurveda, the important factors involved in pathophysiology of any disease are mainly Nidana (etiology), Dosh, Dushya (Dhatu, Srotasa), and Agni. The pathogenesis of COVID-19 can be explained as Bhutabhishhanga (Nidana), leading to vitiation of Tridosha (Dosh). This Bhuta (coronavirus) has a typical affinity toward Pranavaha Srotasa (Dushya - Srotasa). Pranavaha Srotasa being the carrier of Prana Vayu and Urdhva Vayu, and Avalambaka Kapha, vitiation of Vata and Kapha is dominant in the initial stages of disease.

The vitiated Pitta and Kapha Dosh further vitiate Rakta Dhatu (Dushya - Dhatu), which ultimately causes Shopha (inflammation) in the Pranavaha Srotasa making it more vulnerable to diseases. The presence of comorbidities of other Srotasa further aggravates the Pranavaha Srotodushhti. The vitiation of Tridosha initially vitiates Jatharagni (Agni) resulting in various forms of Jwara on the basis of degree of vitiation and in turn vitiates different Dhatwagni (Agni) in later stages.
The progression of the COVID-19 disease is determined by the magnitude of Bhutabhishanga, extent of vitiation of Dosha, Dushya, and state of Sharira Bala in the patients. The relative classification as per modern medicine and Ayurveda is mentioned in Table 4.

The ancient traditional principles of management in the pandemic diseases can be precisely understood through the integrative method. Acharyas have described performing the Panchakarmas in the initial stage of pandemic conditions, which may resist the viral entry into the body or may reduce viral load in the infected patients. Administration of Rasayanas may interfere in the process of pathogenesis by increasing the immunity and nullifies the viral toxic effects on the body. The Aushadha (drug) therapy may help in completely alleviating the residual viral load and managing the patient as per the clinical manifestations.

Table 4: Relative classification of COVID-19 in modern medicine and Ayurveda

<table>
<thead>
<tr>
<th>S. no</th>
<th>Stage</th>
<th>Modern medicine</th>
<th>Ayurveda</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Asymptomatic</td>
<td>RT-PCR test for SARS CoV-2 positive without any clinical symptoms and signs. Chest imaging normal.</td>
<td>Urakshat Purvarupa (Avyaktam Lakshanam Tesham)</td>
</tr>
<tr>
<td>2</td>
<td>Mild</td>
<td>Symptoms of acute URTI (fever, fatigue, myalgia, cough, sore throat, runny nose, sneezing) or digestive symptoms (nausea, vomiting, abdominal pain, diarrhea). Anosmia (loss of smell) or ageusia (loss of taste) preceding the onset of respiratory symptoms may also observed.</td>
<td>Jwar, Pratisayya, Kasa along with Dushi of Pranavaha Srtoto Moolasthana Hridaya and Mahasrotasa</td>
</tr>
<tr>
<td>3</td>
<td>Moderate</td>
<td>Pneumonia (frequent fever, cough) with no obvious hypoxemia, chest CT with lesions.</td>
<td>Vata Kaphaj Jwara, Urakshat</td>
</tr>
<tr>
<td>4</td>
<td>Severe</td>
<td>Pneumonia with hypoxemia (SpO2 &lt; 92%).</td>
<td>Sannipata Jwara, Pratamaka Shwasa</td>
</tr>
<tr>
<td>5</td>
<td>Critical</td>
<td>Acute respiratory distress syndrome (ARDS), may have shock, encephalopathy, myocardial injury, heart failure, coagulation dysfunction and acute kidney injury.</td>
<td>Sama Sannipata Jwara, Urdhvashwas, and Chhinashwas</td>
</tr>
</tbody>
</table>

The evidence-based findings by contemporary science have played a vital role in precise understanding of the pathogenesis of COVID-19, a new pandemic disease in terms of Ayurveda. The collective understanding about the causative factors, stages of disease, clinical features, and complications of disease makes broad route in the management of COVID-19. Ayurveda has described universal treatment principles in management of Janapadodhwamsa.

Each of the stages of the COVID-19 disease is characterized by the interaction between the different degrees of vitiated Dosha and Dushya (Dhatu and Srotasa) and Agni. While there may be overlapping of stages of disease, it is very important to recognize each stage to prescribe specific management for the patients.

CLINICAL SIGNIFICANCE

The interpretation of pathogenesis of COVID-19 in terms of Ayurveda makes better application of these treatment principles in prevention, reducing the complications, and for successful management of the disease.

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कोविड-19 रोग जनन प्रक्रिया / सम्प्राप्ति-आयुर्वेद के परिपेक्ष्य से एकीकृत एवं सामायिक जान्ति

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कोविड-19 यह विश्व स्वास्थ्य संगठन द्वारा घोषित एक नवीनतम विश्वव्यापी धातक एवं गंभीर महामारी/व्याधि है जो श्वसन प्रणाली से संबंधित कोरोना विशारद (SARS-CoV-2) के संक्रमण से होती है। भारत में भी इस व्याधि का संक्रमण एवं प्रसार बहुत तेजी से हो रहा है। आयुर्विज्ञानिक विचित्रता शास्त्र के वैज्ञानिक कोविड-19 के व्याधिनिकत्व हेतु, संक्रमण के प्रसार एवं रोगजनन प्रक्रिया के मूल्य अध्ययन के आधार पर औषधि एवं व्यापक विचित्रता निर्देशों को विकसित करने हेतु प्रयत्नकाल हैं। आयुर्वेद शास्त्र में व्याधी विचित्रता हेतु निदान पंचक एवं द्वारकाकाल का रोग परिजन के संदर्भ में अनन्यसाधारण महत्व है।

तथा नवीनतम से अपरिचित व्याधियों की चिकित्सा हेतु यह जान दिशा दर्शक होता है। प्रत्युत्तम समीक्षा का हेतु आयुर्विज्ञान इंट्रिक्षुण से कोविड-19 व्याधि की व्याधिनिकत्व प्रक्रिया को प्रतिपादित करना है। आयुर्वेद शास्त्र के अनुसार कोविड-19 इस विश्वव्यापी महामारी का अन्तभांव “जनमदृष्टि” व्याधियों में होता है। आयुर्वेद में सूक्ष्म विशारदों/जीवाणुओं का वर्तमान भूत, रक्षा, यहां के परिपेक्ष्य प्राप्त होता है जो अपनी कृतितकित्व के अनुसूच व्याधि उत्पन्न करते हैं। अतः कोरोना विशारद की तुलना एक विशेष प्रवर्तक के “भूत” से की गी संकल्प है जो अतिरिक्त सोतस से संबंधित कर भूताभिन्न, ज्वर (एक प्रकार के अयंतु ज्वर) उत्पन्न करता है। इस व्याधि की उत्तरकलीन अवस्था में यह मिश्र व्याधि में स्प्रंशित होकर तरतमयाविभाग से अंशांश विद्वेष दृष्टि के परिश्रमस्वरूप शरीर में मुख्यतः विचित्रता प्रकार के उपर एवं अन्यत्तिकित प्रमाण में प्राप्त व्याधि सोतिक्षुनिर्माण विकारों की उत्पत्ति होती है। आयुर्वेद शास्त्र में व्याधी जीवन प्रक्रियाओं, दोष, दृष्टि (धातु एवं सोतस) तथा अर्क का जान पारस्परिक स्व से व्याधि के विकर्मित परिवर्तन एवं तीनाक्षर से संबंधित होता है। उपरोक्त प्रकारक निर्विरोधतत्त्वों के अंशांश दृष्टि का जान व्याधित अवयुक्त व्याधि निदान एवं चिकित्सार्थ अर्क/परम आवश्यक है। कोविड-19 व्याधि के आयुर्विज्ञान व्याधिनिकत्व की अवधारणा स्थापित करने हेतु आयुर्वेद एवं आयुर्विज्ञान शास्त्र का सम्मिलित अध्ययन अत्यंत महत्वपूर्ण है।