



AYURVEDA PERSPECTIVES OF COVID-19

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Abstract: COVID-19 outbreak due to SARS-CoV-2 is caused a pandemic condition globally with thousands of deaths and millions of infectees, as well directly affected to the global economy in a deadly way. Being a viral born disease, an effective medicine for the disease is still unknown. Therefore, an effective medicine is highly essential to eradicate the prevailing outbreak. Based on the holistic science of Ayurveda, treatment modalities are built up with the basis of dosha dushya sammurchana of the disease. Hence, a tangible study through existing literature in an inductive way with a critical analysis has been elaborated strong sense towards the etiopathogenesis and pathophysiology of the disease comparing to Sukshma krimi janya vata kapha jvara at the mild to moderate condition and in severe stage as the kapha pradhana sannipata jvara. The theory of shatkriyakala in Ayurveda depicts an extensive concept to build up a treatment protocol with suggestive management system to battle against COVID-19 through specific antiviral medicine and immunomodulators. Therefore, prevention, management and health promotion against COVID-19 is suggested through the Ayurveda perspective.

Index Terms - COVID-19, jvara, krimi, immunomodulator, janapadodhwamsa.

I. INTRODUCTION

The current outbreak of Coronavirus Infectious Disease 2019 (COVID-19) which caused by severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has been inflated a pandemic situation worldwide (WHO, 2019). World Health Organization (WHO) commends that the interim name of the disease causing the current outbreak should be "2019-nCoV Acute Respiratory Disease" ('n' denotes novel and 'CoV' denotes Coronavirus) (WHO, 2020).

Latest statistics on COVID-19 highlight that more than 126 millions of people have been infected globally while more than 2.7 million among them were dead. As well, more than 102 million of cases were recovered totally (Worldometers, 2021). Epidemiology unit of Ministry of Health and Indigenous Medical Services has reported that more than 91,000 cases who have been found positive with COVID-19, while more than 88,000 of them are totally recovered with more than 550 deaths (Epidemiology Unit, 2021).

Allopathy medicine plays a great role in prevention from COVID-19 and public health promotion, as well as management of complications through Allopathy is progressing on. Even though, a successful treatment modality against the condition is still not identified. Management of complications and guidelines for prevention leads to prevalence (Worldometers, 2021). In absence of effective remedy for COVID-19 in modern medical sciences, the time has come to search through indigenous medical knowledge systems to find out an efficient management/treatment protocol.

It is worth to pay an attention towards Chinese health system to get an idea about their treatment approach for COVID-19, because China is successful in combating this endemic within a short time despite the number of cases and mortality rate of. Based on the experience in prevention of SARS and H1 N1 using traditional medicine China used a traditional and integrated approach in addressing COVID-19 (Epidemiology Unit, 2021).

As a holistic system of science, Ayurveda plays a great role in disease prevention and health promotion of individuals. Ayurveda treatments are based on a scientific knowledge of pathophysiology. Acharya Charaka, a great scholar of Ayurveda describes in case of newly oriented disease, the physician should rationally construct the etiopathogenesis (samprapti) or the pathologic physiology of an abnormal clinical picture based on the basic principles, etiology, symptomatology, and method of investigation for the proper management (Arunachalam, 2004). Thus, reveals the importance of review on newly introduced diseases through Ayurveda perspective to find out a proper management protocol to address challenging health needs using aforementioned methodology of Acharya Charaka.

The current study based on a critical review regarding COVID-19 through Ayurveda perspective to address effective management protocol for the condition referring a slogan of Acharya Charaka 'complete knowledge cannot be obtained by knowing the fragmentary knowledge' (Shukla, 2002).

II. AIMS AND OBJECTIVES

The study aimed to critically review etiopathogenesis and pathophysiology or element of diagnosis (samprapti ghataka) of COVID-19 through the Ayurveda perspective including exact etiology, site of the manifestation (udhbhava sthana), involvement and communication of body humors (sanchara), affected organs (avayava and adhishtana) and effects to human body (dosha dushya sammurchana and sroto dushti).

2. METHODOLOGY

The study was conducted in two ways through a literature review and critical analysis of existing information comparing modern pathological discussions with traditional knowledge. The literary review was referred through authentic Ayurveda classics such as Charaka Samhita (CS), Sushruta Samhita (SS), Ashtanga Hrudaya Samhita (AHS) and Madava Nidana (MN).

The review on COVID-19 was conducted through recent scientific explanations and findings which published in official websites and indexed journals, articles, reports of WHO and encyclopedias. The gathered information was compared with traditional and modern scientific explanations using etiopathogenesis, symptomatology, pathophysiology and expected complications.

3. DISEASE REVIEW

Corona virus is commonly found as a pathogen that affects to both of human and animals. As a virus of microscopic visibility, discussion on Ayurveda Krimi roga is much advantageous at COVID-19. Both of visible or invisible worms and microbes are considered under krimi in Ayurveda. According to the classification of Krimi in Vedic literature, Atharvaveda and 19th stanza of 54th Chapter in SS describes that two types of Krimi are available as visible (Drishya) and invisible (Adrushya).

3.1 Etiology

Origin of Coronavirus is still unknown according to the modern sciences, though the classic AS explains that krimi are present all over the biosphere including animals, water, plants and land [7].

The report of the WHO-China joint mission on COVID-19 highlights that the COVID-19 virus is a new pathogen which is highly contagious and spread among people due to lack of respiratory hygiene [8]. The Atharvaveda highlights that the lack of hygiene is the etiology for krimi roga and responsible for the origin of 'Kururu', 'Alagandu' and 'Shaluna' diseases; as well as, the classic mentions that the Rajayakshma (Tuberculosis) is a krimi origin disease which is highly contagious [7]. Therefore, the concept of Atharvaveda (AV) denotes positive regards towards the WHO explanation of spreading and etiology and the key etiological factor for COVID-19 is considered as the infection of novel Coronavirus.

As well, CS explains that, mucosal tissues (Kleda) in the body are one of special location for origin of Krimi. Similarly, the COVID-19 virus was subsequently detected and isolated in lungs and intestinal tissues of affected people [8]. It has been proved that the virus was found even in fecal swabs and blood; indicating the possibility of multiple routes transmission due to presence of Angiotensin Converting Enzyme 2 (ACE2) proteins in epithelial cells of lung alveolar and enterocytes of small intestine [9, 10, 11].

Synonyms for Krimi mentioned in authentic classics are providing positive evidences to prove the aforementioned concept of etiology, such as; AV used following synonyms for Krimi,

Rakshas: the organism which is a parasite of man (Atharva Veda 5/23/1) [7] thus denotes prevention from the infection refraining human to human transmission [12];

Anva: a microscopic organism [7];

Pishacha: which eat raw flesh (vachspaty) [7] that means the microorganism is living inside of the body flesh whereas respiratory tract, because ACE2 found in the lower respiratory tract of humans including alveolar site is known as the cell receptor for COVID-19 [13];

Yatudhana: which cause pain (sabdakalpadruma) [7] because fatigue, sore throat, headache and generalized physical weakness occur at the infection [14];

Kimidi: which can penetrate (nirukta 6/11) [7], this elaborates the viral replication and pathogenesis. According to the recent findings, ACE2 on the surface of human cells act as the cellular entry receptor of the virion S-glycoprotein on the surface of SARS-CoV-2 [15, 16]

After Vedic era, Krimi has been discussed in Samhita literature, details of Krimiroga is found in CS Vimansthana, in the parlance of Krimija Hridroga & Shirashoola, and indirectly in Janapadodhwamsa chapter. In SS, description of Krimi is found in Krimiroga Nidana and Chikitsha. SS describes that infestations of Krimi responsible in Upasargika Roga which means it is a contagious disease, where infection occur and microbes is responsible for it, from this it can say that Krimi is responsible for contagious diseases [17].

3.2 Clinical Importance of Krimi Roga

The commentary for CS, Ayurveda Dipika of Chakrapani describes infestations of Krimi which resides in human body invading tissues and locate in particular sites resulting production of various diseases [18]. Fever (Jvara), discoloration of part or whole body (Vivarnata), colic (Shula), cardiac diseases (Hrud Roga), vomiting (Chardi), giddiness (Bhrama), aversion towards food (Bhaktadvesha) and diarrhea (Atisara) are mentioned in Ayurveda Classics as the complications of krimi infestations [18]. Among aforementioned complications, fever is much common in COVID-19 [8]. In case of viral infection, body temperature is getting increased to destabilize viral RNA polymerase. Hence, there are some positive evidences regarding the molecular changes on the pathogen in elevated body temperature, especially over gene expressions and conformational changes which affect RNA structures and viral replication process [19, 20].

3.3 The Transmission of Pandemic Diseases

Ayurveda perspective on contagious diseases is widely discussed in Janapadodhwamsa chapter of CS Vimansthana. The Janapadodhwamsa means pandemic conditions which cause destruction of human colonies. As per that SS highlights, fever (Jvara), skin diseases (Kushta), tuberculosis (Shosha) and conjunctivitis (Netrabhishyanda) are considered as pandemics [18]. As an

epidemiological disease, ongoing outbreak of coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) has elicited a global pandemic situation. The pandemic declaration was stated on March 11, 2020 WHO aftermath, declaration it is as Public Health Emergency of International Concern (PHEIC) on January 30, 2020 [21]. SS discusses on Sankramika roga as communicable diseases which may responsible in mass destructions of human colonies likely epidemic disorders. Epidemiological diseases spread among people due to exposure or closed contact (even in sexual contact) can, touch of body parts, inhalation of others exhaling breath, eating together, sleeping together and consuming common clothes, jewelry and cosmetics etc. [22]. Comparing to modern knowledge on transmission of communicable diseases, the explanation given in SS can be categorized in 3 ways as through skin, nasal, and faecoral routes. According to the WHO, COVID-19 demonstrates 3 methods of transmissions likely symptomatic transmission, pre-symptomatic transmission and asymptomatic transmission. The symptomatic transmission refers transmission the disease from person to person within first three days onset of symptoms. Contamination through respiratory droplets and direct contact of contaminated surfaces lead to transmit the disease through nasal route. In pre-symptomatic transmission, the diseases transmit person to person while incubation period averagely from 5-6 to 14 days prior to experience symptoms. WHO highlights that the pre-symptomatic transmission still requires the virus to be spread via infectious droplets or through touching contaminated surfaces which confirms the transmission through nasal route. The asymptomatic transmission is still doubtful due to transmission of the disease from a person who has not experiencing any of symptoms [23]. According to SS, COVID-19 confirms the transmission through closed contacts such as inhalation of others exhaling breath or contacts with contaminated objects with respiratory droplets. Ayurveda authentic texts have been discussed the preventive measures from communicable diseases under sadvrutta chapters. As per that, Nidanasthana 5th chapter of SS describes to avoid from close contacts with people who are suspected or infected with diseases highlighting the causes for aupasargika roga [22]. In Janapadodwamsaniya Adhyaya of CS highlights that triggering factors for the epidemic diseases as Vayu, Udak, Desha, and Kala likely pollution of air, water, land and seasonal changes respectively. People who are having less bala (strength against diseases) are easily got infected. Indriyopakramaniya Adhyaya of CS Sutrasthana mentions that personal hygiene is excessively needful to refrain from infectious diseases, as well as proper psychological practice will keep people from diseases. The most important instruction given by CS is maintaining social distance up to six feet while maintaining contacts [18].

3.4 Pathogenesis

The Ayurvedic perspectives on existence of pathogenic virus and a viral infected disease introduced as a Bhutabhisanga disease under sahakari karanas (accessary, exciting exogenous causes with intellectual blasphemery). A person afflicted with Bhutabhisanga usually reinforces abnormalities in body humors likely vatadi tridosha, rasadi dhatus and trimala (mutra, purisha, sweda). Therefore, Ayurveda confirms that communicable diseases like COVID-19 cannot develop independently [24].

In SS, pathogenesis is widely discuss according to the concept of six stages of disease forming (Shatkriyakala) [25]. Shatkriyakala elaborates an idea on affect over body humors and tissues (dosha dushya sammurchana) and progress of the disease inside the body. Sanchaya (accumilation), Prakopa (aggregation), Prasara (transmission), Sthana Samshraya (localization), Vyakti (manifestation) and Bheda (differentiation) are the six-component included in Shatkriyakala process.

Being the etiology for COVID-19, krimi plays a great role in disease forming. According to the AV, krimi infestations cause a contagious condition named Rajayakshma and transmission was occurred with birds. As well as the 5th stanza of 5th chapter of Cikitsa sthana in CS highlights that the rajayakshma is spreading with respiratory droplets (yakshma). This evidence is much related with the evidence of zoonotic origin in SARS-CoV-2 which transmits to humans. Previous studies have suggested that Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and Middle East Respiratory Syndrome Coronavirus (MERS-CoV) are originated from bats [26]. Though the modern zoology introduce bat as a mamal instead of being a bird due to having mammary glands and adapted forelimbs generates wings.

SARS-CoV-2 is suggested to be entered to the human cells through ACE2 receptors. Therefore, ACE2 hormone is unable to bind with ACE2 receptors and cause lack of antibodies secretion to identify the pathogen. This reveals that the virus generates a molecular phishing scam to sneak into the host cell by declining stress response of the body. Thereafter, the virus moderate the genetic reproduction of cell membrane and begin viral replication. As a result, the originated viruses are getting burst out from the host cell and transmit to other particular locations [27]. While the aforesaid process, the body begins to regenerate immune response against the viral process and stimulate the production of Interleukin 6 (IL-6) by activating leukocytes and acute phase proteins which responsible in anti-inflammatory activity and thermoregulation of the body. IL-6 increases during infective diseases and implicate into the pathogenesis of the Cytokine Release Syndrome (CRS) characterized by fever and multiple organ dysfunction [28].

Similarly, Shatkriyakala concept can be used in the explanation of Ayurveda perspective on pathogenesis. Though due to key exogenous etiologies like as krimi (virus) infection, the sanchaya stage will not be much prominent. People with less vyadhikshamatva due to the ama condition are easily affected with krimi invasions. In less ama condition, dosha sanchaya (accumilation) is much possible comparing with nirama condition. In nirama, who are having less vyadhikshamatwa are directly move to the prakopa stage. Therefore, aggregation of particular dosha are getting activated.

3.4.1 Sanchaya (Stage of Accumulation)

Accumilation of vitiated doshas in their particular location is called as sanchaya [29]. Due to the viral (krimi) infestation, the virus excretes inflammatory agents to both of intracellular and extracellular spaces and cause inflammation. Therefore, stimulation of IL-6 and acute phase protein production is activated with the messenger like and transportation like involvement of vata dosha. The produced IL-6, acute proteins and other substances are released with the involvement of pitta dosha. Meanwhile secretions and bindings and receptions are generated with the kapha dosha. At the occasion of the viral invasion, the aforementioned process is getting accelerated and all the three humors (vata, pitta and kapha) involved in their function excessively which generate accumulation of above doshas in their particular site where the infection occurs likely upper respiratory tract.

Dosha sanchaya is increased due to involvement of three types of causative factors (thrividha hetu) (TH) basically as intellectual blasphemery (Pragnaparadha), misleading of sensory organs (Asatmendriyartha samyoga) and inherent causes (Parinama). Etiological factors for Aupasargika roga mentioned in SS, are directly involve in Pragnaparadha and Asatmendriyartha samyoga [22]. Being a kapha predominant tract, upper portion of pranavaha srotas (upper respiratory tract) and upper portion of rasa vaha srotas (upper alimentary channel) are the vulnerable site of dosha acumilation. Excessive involvement of vata dosha and kapha dosha cause dosha

sanchaya in COVID-19 infection. Asymptomatic infection which highlights by the WHO is much correlated with the sanchaya stage like as incubation period [8].

Considering the Krimi etiology, in sanchaya stage, the treatment procedure should be based on refrain from etiological factors. Therefore, Krimi Apakarshana (physical removal of microbes), Prakrutivighata (antagonistic measures) and Nidana parivarjana (avoid from etiologies) should be followed. In Krimi Apakarshana, the concept to use antimicrobial applications in externally is applicable as WHO such as alcohol base hand rubs and soap etc [8]. For this, Ayurveda instructs to use Ferula foetida oligo gum resin, rhizome of *Curcuma longa*, *Coscinum fenestratum*, leaves of *Azadirachta indica* and leaves and fruit juice of plants in Rutaceae family. Even after the Krimi Apakarshana, residues of krimi may remaining in the body, hence for the further elimination Prakrutivighata is advised. In Prakrutivighata, medicinal and diet application to avoid krimi development is advised. Therefore, the factors favourable to krimi development such as kapha predominant properties likely sheeta (cold), snigdha (oily) and madhura rasa (sweet in taste) should be removed. Hence, antiviral drugs consisting with katu (punjent), kasaya (astringent), tikta (bitter) tastes and rooksha (rough), ushna (hot in potency), laghu (light in properties), such as Zingiber officinale, Acorus calamus, *Coscinum fenestratum*, Ferula asafetida oligo gum resin are recommended. In nidana parivarjana, avoid of closed contact which mention under aupsargika roga in SS are much applicable comparing to the concept of WHO [8, 22, 30].

In this stage, the infected individual should be treated referring Samanya Vishesha concept (SVC) mentions in CS. As SVC, the case should be treated recognizing dosha vrudhdhita (inclined doshas) and dosha kshinata (declined doshas). Therefore, substances having opposite properties to vata and kapha dosha are much beneficial such as Ushan guna, Katu rasa and Theekshana ingredients are applicable. Zingiber officinale, Acorus calamus, *Coscinum fenestratum* and Piper nigrum are recommended [31]. Improper guidance of TH leads sanchaya to prakopa stage.

3.4.2 Prakopa (Stage of Aggregation)

Further accumulation of vitiated doshas in the particular location is known as Prakopa. According to the Dalhana commentary of SS, the accumulated doshas are getting melted in this stage to get ready for the transmission in upcoming stage [32]. Further consumption of TH correspondances on COVID-19 lead to aggregation of vitiated doshas in particular sites. The prakopa stage consists with two sub stages as chaya prakopa and achaya prakopa. In chaya prakopa physiological aggregation of doshas can be observed due to natural reasons such as close contact of infected individuals, associated disease conditions such as asthma, pneumonia, tuberculosis, tonsillitis, adenoditis and common cold etc. Additionally, seasonal changes probably exposure to rainy season, exposure to heavy dust and allergens challenge to immune system with inflammations. Recurrent exposure to inflammations leads to lack of immunity (Vyadhikshamatva) and host for infective diseases like COVID-19. In achaya prakopa, acute condition of dosha vitiation can be observed likely exposure to cold wind and engage in heavy works etc. Being a krimi infestation, COVID-19 characteristic with fever, therefore sanjatha krimi lakshana consists with jvara as well as pratishya and kasa conditions, thus compared with modern and Ayurveda concept. Among general etiology for jvara mentions in SS as, over exertion, depletion of dhatu, indigestion, toxins due to end products of physiological or pathological reaction, after an inflammatory process, injudicious use of diet etc. are included under achaya prakopa related to COVID-19 [33]. Compared with SS, the CS, AHS and MN mentions specially over exertion is the leading cause for jvara [34]. In this prakopa stage, patients begin to show signs and symptoms relevant to COVID-19 such as fever, dry cough, fatigue, sputum production, shortness of breath, sore throat, headache, myalgia or arthralgia, chills, nausea and vomiting, nasal congestion, diarrhea, hemoptysis and conjunctival congestion [8]. The symptomatic transmission of COVID-19 begins in this stage. Polymer Chain Reaction (PCR) test is much applicable in this stage as a diagnostic tool because the pratishya and kasa conditions are initially associated with ama samsargaja conditions due to vitiation of kapha. Therefore, Ama pachana and kaphaghna treatments are much beneficial in this stage. As well, the treatment protocol should be aligned with prakruti vighata considering the altered status of particular doshas. To reduce the virility of coronavirus bshesaja apakarshana (disinfection of krimi using medications) is much beneficial.

3.4.3 Prasara (Stage of Transmission)

Aggregated doshas of prakopa stage get melted with the affliction of kapha dosha according to the Dalhana Acharya and transmit through particular srotas (channels) to other body parts leaving the location of origin with the affliction of vata dosha is occurred in prasara stage. Furthermore, the liquified vitiated doshas are getting amalgamated with other related doshas and cause excessive flow (Atipravrutti sroto dushti). As a result of that, the flow directed over the internal viscera (Abhyantara roga marga) such as alveoli structures of the lungs, pleura, bronchial tree and intestines etc. The transmission and liquification of accumulated and aggregated doshas are conducted through the properties of vitiated vata and kapha doshas respectively [35].

Therefore, sputum production, shortness of breath, sore throat, nausea and vomiting, diarrhea and hemoptysis is gradually increased. Furthermore, development of non-productive cough and fever can be observed [8]. In this stage, COVID-19 patients mostly positive with Vata kapha jvara lakshana (clinical features). Stagnation of oversecreted mucus over the bronchus cause narrowing of the bronchial lumen and results in difficulty in breathing associated with productive cough or wheezing.

Table 1: *Vata kapha Jvara Lakshana* (Clinical features) according to Ayurveda Authentic texts

Clinical Features of <i>Vata kapha jvara</i>	CS	SS	AHS	MN
<i>Sheeta</i> (Feeling of cold)	+	-	+	-
<i>Gaurava</i> (Heaviness in the body)	+	+	-	+
<i>Tandra</i> (Drowsiness)	+	-	-	-
<i>Staimitya</i> (Timidity, stiffness as if covered by a wet cloth)	+	-	-	+
<i>Parva ruk</i> (Pain in interphalangeal joints)	+	-	-	
<i>Shirograha</i> (Rigidity of head)	+	-	-	+
<i>Pratishya</i> (Common cold)	+	+		+
<i>Kasa</i> (Cough)	+	+	+	
<i>Asweda</i> (Absence of sweating)	+	+	-	-
<i>Madhya vega santapa</i> (Moderate rise in temperature)	+	+	+	+

Aruchi (Anorexia)	-	-	+	
Puruk shula (Pain in joints)	-	+	+	+
Shirashula (Headache)	-	+	+	-
Pinasa (Catarrh)	-	-	+	-
Shwasa (Dyspnea)	-	-	+	-
Mala-Mutra Baddhata (Difficult in urination and defecation)	-	-	+	-
Darkness in the sight	-	-	+	-
Bhrama (Giddiness)	-	-	+	-
Jadyata (Stiffness of the body)	-	-	+	-
Tandra (fatigue)	-	+	+	-
Nidra (Excess sleep)	-	-	-	+
Sweda pravartana (Excessive perspiration)	-	-	-	+

Up to 20th of February 2020, WHO highlights that among 55924 of diagnosed COVID-19 cases, fever (87.9%), dry cough (67.7%), fatigue (38.1%), sputum production (33.4%), shortness of breath (18.6%), sore throat (13.9%), headache (13.6%), myalgia or arthralgia (14.8%), chills (11.4%), nausea or vomiting (5.0%), nasal congestion (4.8%), diarrhea (3.7%) and hemoptysis (0.9%) and conjunctival congestion (0.8%) were found as clinical features [8].

Additionally, fever, dry cough, fatigue, myalgia, dyspnea, anorexia [36] [37] and diarrhea [38] could be introduced as common symptoms of COVID-19 and as fewer common symptoms confusion, muscle ache, headache, sore throat, rhinorrhea, chest pain, sputum production [38] and nausea and vomiting [37] could be highlighted. As well, another study highlights that fever and cough were the dominant symptoms and diarrhea was uncommon [39].

Table 2: Vata kapha Jvara Lakshana (Clinical features) vis á vis clinical features of COVID-19

Clinical Features of Vata kapha jvara	CS	SS	AHS	MN	COVID-19
Sheeta (Feeling of cold)	+	-	+	-	+
Gaurava (Heaviness in the body)	+	+	-	+	+
Tandra (Drowsiness)	+	-	-	-	+
Staimitya (Timidity)	+	-	-	+	+
Parva ruk (Pain in interphalangeal joints)	+	-	-	-	+
Shirograha (Rigidity of head)	+	-	-	+	+
Pratishya (Common cold)	+	+	-	+	+
Kasa (Cough)	+	+	+	-	+
Asweda (Absence of sweating)	+	+	-	-	-
Madhya vega santapa (Moderate rise in temperature)	+	+	+	+	+
Aruchi (Anorexia)	-	-	+	-	+
Puruk shula (Pain in joints)	-	+	+	+	+
Shirashula (Headache)	-	+	+	-	+
Pinasa (Catarrh)	-	-	+	-	+
Shwasa (Dyspnea)	-	-	+	-	+
Mala-Mutra Baddhata (Difficult in urination and defecation)	-	-	+	-	diarrhea
Darkness in the sight	-	-	+	-	-
Bhrama (Giddiness)	-	-	+	-	-
Jadyata (Stiffness of the body)	-	-	+	-	+
Tandra (fatigue)	-	+	+	-	+
Nidra (Excess sleep)	-	-	-	+	-
Sweda pravartana (Excessive perspiration)	-	-	-	+	-

3.4.4 Sthana Samshraya (Stage of localization)

In this stage, the transmitting aggravated doshas are getting located other than the particular location of origin due to Sangha sroto vaigunya (obstruction of transmitting channel). Therefore, a disease manifestation in localized sites can be observed. In Sthana Samshraya, process of interaction between morbid elements and tissues are occurred.

The Sroto vaigunya occur in this stage leads to Dosha dushya sammurchana and clinically possible with Prodromal Symptoms specialized to secondary locations [32] such as fever and respiratory symptoms are positive with radiographic changes including non-specific imaging findings with atypical or organizing pneumonia, often with a bilateral, peripheral, and basal predominant distribution [40]. Additionally, lymphopenia, increased prothrombin time and increased lactate dehydrogenase, mild elevation of inflammatory markers {CRP (C – Reactive Protein) and ESR (Erythrocyte Sedimentation Rate) } and D-dimer (a serum investigation to trace venous thromboembolism) can be observed in early stages of the severe stage [41, 42].

The most common finding is airspace opacities and this is mostly extensive about 10 to 12 days after the onset of signs and symptoms [42, 43]. Moving to the symptomatology described in Ayurveda, increase of jvara condition with affliction of pitta is highlighted, as well further inclination of vata and kapha demonstrate shaitya (coldness), kasa (cough), aruchi (anorexia), tandra (drowsiness), pipasa (thirst), daha (burning sensation) and vyata (pain) [44].

Therefore, in this stage *samprapti vighatana* should be applied as the management protocol. Refrain from the TH should be continued to avoid gradual onset into forthcoming stage [32].

According to some of recent studies, in case of fever, prostaglandin E2 is releasing and affect in homeostasis to reset the body temperature in a higher point. As a result of prostaglandin secretion, secretion of Hydrochloric (HCl) is getting deprived in parietal cells of the stomach. Therefore, inactive enzyme pepsinogen is unable to convert into active form of pepsin.

Hence, digestion of proteins into amino acids and antimicrobial action against pathogenic microorganisms in gastrointestinal tract is getting declined. This leads to cause lack of appetite and digestive issues are possible to occur [45]. Treatment protocol for *jvara* mentions that *langhana karma* (applying light diets) is much appropriate in early stages of *jvara* because *langhana* reduces the aggravated *dosha* and stimulate the digestive fire (*Agni*). As a result, *jvara* condition is getting subsided and appetite is getting restored. For this purpose, consumption of boiled water, *dipana* (digestive stimulants), *pachana* (digestive enhancers) and *jvaraghna* (*jvara* alleviators) medicines should be introduced.

Therefore, the *srotas* (channels) are getting cleansed and promote circulation, appetite and *vyadhi kshamatwa* (immunity). Failure to regain digestive fire, *ama* is getting generated inside the stomach and cause much *sroto dushti* which will lead to further complications [46].

3.4.5 Vyakti (Stage of Manifestation)

The manifestation of the disease is conducted in this stage, because clinical features are well produced and related investigations are getting positive. Therefore, the diagnosis is mostly accurate in vyakti avastha. As a severe stage of the disease, dyspnea occurs with Respiratory Rate (RR) equal or greater than 30 times/min, Oxygen saturation equal or less than 93% in ambient air, (Partial Pressure of Oxygen) PaO₂/FiO₂ (Fraction of Inspired Oxygen) ratio less than 300, and/or lung infiltrates >50% of the lung field within 24-48 hours are much common [8]. At the rise of dosha dushya sammurchana, all the three doshas are getting vitiated including dhatus. Therefore, the vata kapha *jvara* condition is getting complicated into sannipata *jvara* condition with following features; shaitya (coldness), kasa (cough), aruchi (anorexia), tandra (drowsiness), pipasa (thirst), daha (burning sensation) and vyata (pain) [44].

In kapha predominant sannipata *jvara*, CS, SS and AHS mentions that a combination of clinical features in each type dosha predominant *jvara* are available in sannipata *jvara* [47].

Table 3: Comparison of clinical features in COVID-19 and *Kapha pradhana sannipata jvara*

Symptoms	CS	SS	AHS	MN	COVID-19
<i>Kshane Daha Kshane Sheeta</i> (Alteration of hotness and coldness)	+	+	+	+	Alteration of fever
<i>Asthi sandhi shiro ruja</i> (difficulty in joints, bones and head)	+	+	+	+	+
<i>Sasrave kalushe rakte nirbhugne chapi lochane</i> (Sunken reddish eyes with discharges)	+	+	+	+	+
<i>Tandra</i> (Drowsiness)	+	+	+	+	+
<i>Moha and Pralapa</i> (Delusion and Delirium)	+	+	+	+	-
<i>Kasa</i> (cough)	+	+	+	+	+
<i>Shvasa</i> (Difficulty in breathing)	+	+	+	+	+
<i>Aruchi</i> (Anorexia)	+	+	+	+	+
<i>Bhrama</i> (Giddiness)	+	+	+	+	+
<i>Paridagdha kharasparsha jihva</i> (Reddish tongue with rough edges)	+	+	+	+	-
<i>Srastangata</i> (Weakness of limbs)	+	+	+	+	+
<i>Shitiwanam rakta pittasya mishra kapha</i> (spitting rusty sputum mixed with bile and blood)	+	+	+	+	Spitting mucus
<i>Shiraso lotane</i> (Rolling the head over the pill)	+	+	+	+	Due to difficulty in breathing
<i>Thrushna</i> (thirst)	+	+	+	+	Possible
<i>Nidranasha</i> (Insomnia)	+	+	+	+	+
<i>Hrudi vyata</i> (Discomfort in heart)	+	+	+	+	+
<i>Sweda mutra purishanam chiraaddarshanamalpashah</i> (lack of sweating, urine output and feces at long intervals)	+	+	+	+	Diarrhea is less common
<i>Gatrasya nathi krushatwam</i> {Less changes in Body Mass Index (BMI)}	+	+	+	+	-
<i>Kanta kujanam</i> (Mourning)	+	+	+	+	+
<i>Kotanam</i> (Dark spots over the skin)	+	+	+	+	-
<i>Srotas paka</i> (Ulceration over orifices)	+	+	+	+	Sore throat
<i>Udara guruvam</i> (Feeling heaviness in abdomen)	+	+	+	+	+
<i>Chirat pakasya doshanam</i> (delayed in returning normalcy)	+	+	+	+	+

In Computed Tomographic (CT) changes of adults, following specialties have been observed [48].

1. Ground-glass opacities (GGO) in bilateral, subpleural, peripheral
2. Crazy paving appearance (GGOs and inter/intra lobular septal thickening)
3. Air space consolidation

4. Bronchovascular thickening in the lesion
5. Traction bronchiectasis

Additionally, pleural effusion occurs as a complication of COVID-19, though it has been reported less occurrence of pleural effusion in less severe conditions comparing to complicated stage (vyakti) [48].

In ultrasonography, following changes have been observed, tending to bilateral and posterobasal predominance [48];

1. Multiple B-lines
Ranging from focal to diffuse with spared areas
Representing thickened subpleural interlobular septa
2. Irregular, thickened pleural line with scattered discontinuities
3. Subpleural consolidation
Associated with a discrete, localized pleural effusion
Avascular with colour flow Doppler interrogation
Hyperemia
4. Alveolar consolidation
Tissue like appearance with dynamic and static air bronchograms

In the vyakti, the treatment modality should be based on lakshanika chikitsa (symptomatic treatment) which follow the basic concept of treatment protocol to sannipata jvara. Furtherly, aggravation of doshas in this stage result in weakening body including immune system and all the physical and psychological functions. Therefore, dosha pachana karma should be applied following langhana karma. Shadanga pana has been introduced in CS as a dosha pachana medicine to alleviate jvara associated with the thirst [45]. In case of excessively weakened patient, langhana is prohibited to ensure the life of patient. Thus, tarpana (nutritional) diets are administered which are prepared using laja saktu (powder of roasted grains) mixed with honey, sugar and fruit juices with jvara alleviating properties [49].

CS instructs to apply medicinal decoctions to patients in this stage after administration of langhana karma for 06 days for the purpose of pachana (stimulation of digestion) or shaman karma (dosha alleviators) by assessing the vital features of the infected case [49]. Poor management of the patient while vyakti stage, the condition will be worsened and upgraded into bheda stage.

3.4.6. Bheda (Stage of differentiation)

Complications are mostly aroused in this stage. Management is much complicated. In this disease will become chirakari (chronic) or asadhya (incurable) due to improper management strategies. Mortality is much possible in bheda stage in mistaken of application atyayika chikitsa. Complications are mostly occur to the individuals in high risk stage who are people aged over 60 years and those with comorbid conditions such as hypertension, diabetes, cardiovascular diseases, chronic respiratory diseases and cancers. In this stage most probably, respiratory failure, septic shock and multiple organ dysfunction or failure occurs [8]. According to CS, patients in this stage are experiencing following symptoms while fluctuation of the jvara condition [50].

1. Kujana (rumbling) sound
2. Vomiting
3. Cheshta (abnormal movements of limbs)
4. Shvasa (Forceful breathing due to difficulty in breathing)
5. Discolouration of body
6. Svinna anga (sweating)
7. Vepatu (trembling)
8. Lihyate muhuh (frequent fainting)
9. Pralapa (delirium)
10. Fluctuation of body temperature
11. Unconsciousness
12. Unexpected rise of body temperature
13. Forceful expulsion of doshas mixed liquid stools with flatulence

Obstructions inside airway passages with stagnant mucous are caused kujana and recurrent productive cough leads to vomiting. Due to the difficulty in breathing, cheshta and forceful breathing may occur, as a result of dyspnea occurs with Respiratory Rate (RR) equal or greater than 30 times/min, Oxygen saturation less than 90% in ambient air leads to hypoxemia with $200 \text{ mm Hg} < \text{PaO}_2 / \text{FiO}_2 \leq 300 \text{ mm Hg}$ with (Positive End-Expiratory Pressure) PEEP or CPAP (continuous positive airway pressure) $\geq 5 \text{ cm H}_2\text{O}$ {mild Acute Respiratory Distress Syndrome (ARDS)}; $100 \text{ mm Hg} < \text{PaO}_2 / \text{FiO}_2 \leq 200 \text{ mm Hg}$ with PEEP $\geq 5 \text{ cm H}_2\text{O}$ (moderate ARDS); $\text{PaO}_2 / \text{FiO}_2 \leq 100 \text{ mm Hg}$ with PEEP $\geq 5 \text{ cm H}_2\text{O}$ (severe ARDS), while PaO_2 is not available, and $\text{SpO}_2 / \text{FiO}_2$ ratio ≤ 315 suggests ARDS [51]. Due to the aforementioned shvasa condition, peripheral anemia may cause following hypoxia. Having COVID-19, segmental dilation and stenosis of the small intestine has been observed, as well degeneration, necrosis, and shedding of the gastrointestinal mucosa of varying degrees were observed while histological studies which are suggesting that the gastrointestinal symptoms of SARS-CoV-2 infection might be caused due to the direct viral attack and tissue/organ damage resulting immune response [52]. In this stage, sepsis associated with organ dysfunction, hypoperfusion (lactic acidosis) and hypotension can be occurred due to temperature $> 38^\circ \text{C}$ (100.4°F) or $< 36^\circ \text{C}$ (96.8°F), Heart Rate (HR) $> 90/\text{min}$, $\text{RR} > 20/\text{min}$ or PaCO_2 . Organs dysfunction in this stage is included; oliguria, acute kidney injury, hypoxemia, transaminitis, coagulopathy, thrombocytopenia, altered mental status, ileus or hyperbilirubemia [51] is highly correlated with the opinion of CS as well as sannipata jvara lakshana mentioned in MN. In an uncontrollable management, septic shock can be occurred with Sepsis-induced hypotension ($\text{SBP} < 90 \text{ mm Hg}$) despite adequate fluid resuscitation and signs of hypoperfusion [51].

As per the atyayika chikitsa for the management of severe respiratory distress, hypoxemia and ARDS, high intrapulmonary shunt fraction is occurred. Therefore, mechanical ventilation (non-invasive or invasive) is required [51]. In pleural effusion, external

applications over thorax with shoshaka guna (absorptive properties) such as root bark of *Moringa oleifera*, rhizome of *Zingiber officinale*, whole plant of *Boerhavia diffusa* and seeds of *Brassica nigra* are much beneficial [53].

3.4.7 Element of Diagnosis (Samprapti Ghataka)

Nidana: Krimi

Dosha: pradhana Avalambhaka Kapha; Anubandhi: Prana, Udana and Vyana Vata with Pachaka Pitta

Dushya: Rasa, Rakta

Agni: Jataragni Mandya

Ama: Sama Vata (Shotha, Vedana)

Udhhava Sthana: Amashaya, Puppusha

Srotas: Pranavah, Rasavaha

Srotodushti: Atipravrutti, Sangha, Vimarga Gamana

Roga Marga: Abhyantara

Adhishtana: Puppusha

4. DISCUSSION

Being a novel disease, COVID-19 causes a pandemic situation globally [2] and an effective medicine against the pathogenic has not been introduced. Therefore, studying the historical evaluation of pandemic situations is advantageous to find out learnt lessons while critical time periods. Ayurveda as a holistic science of human wellbeing has broadly discussed on pandemics including etiopathogenesis, prevention, management and possible complications. At further studies, CS, SS, AHS and MN which are the great authentic texts of Ayurveda elaborate broad sense on aforementioned pandemics. Even before the Samhita period, Veda literature depicts vast knowledge on epidemiological disorders.

Referring historical literature which represent Ayurveda and with the comparison to current co-relations, the etiology for COVID-19 could be introduced as krimi / janthu. According to the clinical features of krimi roga and morphological feature of pathogenic organism, the causative factor can be introduced as kaphaja krimi, though the anatomy of kaphaja krimi has been declared that kaphaja krimi are having macroscopic structures while raktaja krimi are having microscopic structures. Being a kaphaja netra roga, Krimi granthi which correlated with Blepharitis is caused due to krimi infestation [54, 55]. Recent studies discuss that Blepharitis are caused due to viral, bacterial or microscopic parasitic infections [56-58]. Therefore, the causative pathogenic for Blepharitis could be taken as microscopic and the concept of SS on macroscopic feature of kaphaja krimi is getting challenged only considering the microorganism. Though the colonies of the pathogenic in Blepharitis are macroscopic, therefore the concept of SS is acceptable.

Comparing the clinical features of dosha predominance and vitiation, the thorax is the location of Avalambhaka Kapha and which responsible for secretions, gas exchange, surfactant of alveoli etc. as well breathing, cough, functions of pharynx and larynx are conducted through Prana, Udana and Vyana Vata. Pachaka Pitta is responsible in metabolism through manifestation digestive power of stomach. Therefore, vitiation of aforementioned humors directly depicts clinical features comparing to COVID-19.

The current study critically analyzed the etiopathogenesis, symptomatology, pathophysiology and expected complications comparing Ayurveda and modern concepts. The significance of the study can be introduced as suggesting a logical Ayurveda management protocol with the basis of shatkriyakala.

Ayurveda medicines for such kind of pandemic diseases are consisted with anti-viral properties and immunomodulatory properties. Among herbs, *Zingiber officinale*, *Acorus calamus*, *Coscinum fenestratum*, *Ferula asafetida oligo gum resin*, *Curcuma longa*, *Embelia ribes*, *Caesalpinia bonduc*, *Glycyrrhiza glabra*, *Zingiber officinal* and *Azadirachta indica* etc. are consists with antiviral properties specially with blocking agents of ACE2 and GPR 78 receptors of epithelial cells to battle the binding of receptor-binding domain section of SARS-CoV-2. Specially, *Ferula asafetida oligo gum resin* consist with intensive binding energies for ACE2 receptor-binding process, as well as the aforementioned herbs, *Tinospora cordifolia*, *Piper nigrum*, *Piper longum* are effective, as herbal formulas Sudarshana churna, Ratha kalka, Buddharaja kalka, Seetharama Watee etc. are mentioned as effective immunomodulators [59-64].

REFERENCE

- [1]. World Health Organization. Corona Virus Disease (COVID-19) technical guidance: Infection Prevention and Control/ WASH. [ONLINE] Available at: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/infection-prevention-and-control>
- [2]. World Health Organization. Novel Coronavirus (2019-nCoV): Situation Report – 10. [ONLINE] Available at: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200130-sitrep-10-ncov.pdf?sfvrsn=d0b2e480_2
- [3]. Worldometers, Coronavirus Cases: (2021, March 26). Retrieved 12.17 GMT March 26, 2021, from <https://www.worldometers.info/coronavirus/>
- [4]. Epidemiology Unit. Coronavirus disease 2019 (COVID-19)-Situation Report-26.03.2021-10.00 am. Ministry of Health & Indigenous Medical Services, Colombo Sri Lanka. [ONLINE] Available at: http://www.epid.gov.lk/web/images/pdf/corona_virus_report/sitrep-sl-en-13-04_10.pdf [Access on March 26, 2021]
- [5]. Arunachalam, S. Treatise on Ayurveda. New Delhi: Diamond Pocket Publishers, 2004; p. 128-129.
- [6]. Shukla V, Tripathi R, editor, Charaka Samhita of Charaka, Vimana Sthana, Chapter 4, verses 5, 1st ed, Vol. I, New Delhi: Chaukhamba Sanskrit Pratishtan, 2002, p. 582.
- [7]. Shastri RG, editor, Vedo me Ayurved of Dwivedi KD. Delhi: Printing Works, 1956; p. 49-66.
- [8]. World Health Organization. Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). [ONLINE] Available at: <https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf>
- [9]. Zhang W, Du RH, Li B, Zheng XS, Yang XL, Hu B, et al. Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. *Emerg Microbes Infect*, 2020; 9(1): 386-389.

- [10]. Hamming I, Timens W, Bulthuis ML, Lely AT, Navis G, van Goor H. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus: a first step in understanding SARS pathogenesis. *J Pathol*, 2004, 203(2): 631-637.
- [11]. Guo YR, Cao QD, Hong ZS, Tan YY, Chen SD, Jin HJ, Tan KS, Wang DY, Yan Y. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak – an update on the status. *Milit Med Res*, 2020; 7(11): 1-10.
- [12]. Wan Y, Shang J, Graham R, Baric RS, Li F. Receptor recognition by novel coronavirus from Wuhan: an analysis based on decade-long structural studies of SARS. *J Virol*, 2020. <https://doi.org/10.1128/JVI.00127-20> [Epub ahead of print].
- [13]. Jia HP, Look DC, Shi L, Hickey M, Pewe L, Netland J, et al. ACE2 receptor expression and severe acute respiratory syndrome coronavirus infection depend on differentiation of human airway epithelia. *J Virol*, 2005; 79(23): 14614-14621.
- [14]. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*, 2020. <https://doi.org/10.1056/NEJMoa2002032>.
- [15]. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*, 2020. <https://doi.org/10.1038/s41586-020-2012-7>.
- [16]. Tortorici MA, Veesler D. Structural insights into coronavirus entry. *Adv Virus Res*, 2019; 105:93–116.
- [17]. Shastri A. editor. *Sushruta Samhita of Sushruta, Nidanasthana, Chapter 5, verse 33*. Varanasi: Chaukhambha Sanskrit Samsthana; reprint 2012; p. 325.
- [18]. Trikamaji Y. editor. *Commentary: Ayurveda Dipika of Chakrapani on Charaka Samhita of Charaka, Vimanasthana, Chapter 7, Vers 9, 1st ed*. Varanasi: Chaukhambha Sanskrit Sansthan, 2013; p. 258.
- [19]. Scholtissek C, Rott R. Effect of temperature on the multiplication of an Influenza virus. *J Gen Virol*, 1969; 5(2): 283-290.
- [20]. Alexander DJ, Brown IH. Recent zoonoses caused by Influenza A viruses. *Rev Sci Tech*, 2000; 19(1): 197-225.
- [21]. Epidemiology Unit. Coronavirus disease 2019 (COVID-19)-Situation Report-13.04.2020-10.00 am. Ministry of Health & Indigenous Medical Services, Colombo Sri Lanka. [ONLINE] [Access on April 13, 2020] Available at: http://www.epid.gov.lk/web/images/pdf/corona_virus_report/sitrep-sl-en-13-04_10.pdf
- [22]. Buddhadasa R. *Susruta Samhita, Sinhala translation. Uttarasthana, Chapter39, Verse 49*. Colombo: Educational Department, 1962; p. 788.
- [23]. World Health Organization. Coronavirus disease 2019 (COVID-19) situation report-73. [ONLINE] Accessed on 19.04.2020, Available at: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200402-sitrep-73-covid-19.pdf?sfvrsn=5ae25bc7_2
- [24]. Murthy KRS. *Doctrines of Pathology in Ayurveda*. Delhi: Chaukhamba Orientalia, Varanasi, 2003; p. 25-26.
- [25]. Trikamaji Y. editor. *Sushruta Samhita of Sushruta with Nibandha Samgraha Commentary, 9th edi*. Varanasi: Chaukhambha Orientalia, 2007; p. 103.
- [26]. Hu B, Ge X, Wang LF, Shi Z. Bat origin of human coronaviruses. *Virol J*, 2015; 12(221): 1-10.
- [27]. Foley KE. The coronavirus's survival mechanism is what makes it so dangerous. *Quartz*, March 25, 2020. [ONLINE] Accessed on 19.04.2020 Available at: <https://qz.com/1822554/how-the-coronavirus-tricks-cells-into-a-full-body-invasion/>
- [28]. Cascella M, Rajnik M, Cuomo A, Dulebohn SC, Napoli RD. Features, Evaluation and Treatment Coronavirus (COVID-19) [Updated 2020 Apr 06]. *Statpearls* [ONLINE] Available at: <https://www.ncbi.nlm.nih.gov/books/NBK554776/>
- [29]. Shastri KA. editor. *Sushruta Samhita of Sushruta, Vol I, Sutrasthana, Chapter 21*. Varanasi: Chaukhambha Sanskrit Prakashan, 2004; p. 90.
- [30]. Archana TP, Prashasth MJ, Muralidhar M. Review on Trividha Chikitsa in Krimi Roga: a Conceptual Study. *Int Ayur Med J*, 2015; 3(2): 587-593.
- [31]. Pandey K, Chaturvedi G. *Vidyotini Commentary of Charaka Samhita of Agnivesha, reprint, Vol I*. Varanasi: Chaukhambha Bharati Academy, 2008; p. 15.
- [32]. Joshi R, Joshi VR. *Shatkriyakala Clinical Approach*. *World J Pharma Med Res*, 2019; 5(2): 125-128.
- [33]. Trikamaji Y. editor. *Sushruta Samhita of Sushruta, 7th ed, Jvara nidana*. Varanasi: Chaukhambha Sanskrit Samsthan, 2002; p. 642 & 824.
- [34]. Nagaraj S, Nidhin V. A study of Vishamajvara nidana wsr to risk factors in Malarial fever. *Int Ayur Med J*, 2015; 3(8): 2318-2325.
- [35]. Mastamardi VB. *Ayurvediya Roga Vigyan evum Vikruti Vigyan, Vol I*. Varanasi: Chaukhambha Visva Bharati, 2017; p. 122.
- [36]. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 hospitalized patients with 2019 Novel Coronavirus- infected pneumonia in Wuhan, China. *JAMA*, 2020. <https://doi.org/10001/jama.2020.1585>
- [37]. Chen N, Zhau M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 Novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020; 395(10223): 507-513.
- [38]. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 Novel Corona Virus in Wuhan, china. *Lancet*, 2020; 395(10223): 495-506.
- [39]. Guan W-J, Ni Z-Y, Hu Y, et al. Clinical Characteristics of 2019 Novel Corona virus infection in China. *MedRxiv*, 2020: <https://doi.org/10.1101/2020.02.06.20020974>
- [40]. Kanne JP, Little BP, Chung JH, Elicker BM, Ketai LH. Essentials for Radiologists on COVID-19: an Update-Radiology Scientific Expert Panel. *Radiology*, 2020: <https://doi.org/10.1148/radiol.2020020527>
- [41]. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y, Zhao Y, Li Y, Wang X, Peng Z. Clinical characteristics of 138 hospitalized patients with 2019 Novel Coronavirus infected Pneumonia in Wuhan, China, *JAMA*, 2020: <https://doi.org/10.1001/jama.2020.1585>
- [42]. Rodrigues JCL. An update on COVID-19 for the radiologist-A British Society of Thoracic Imaging Statement. *Clin Radiol*, 2020: <https://doi.org/10.1016/j.crad.2020.03.003>
- [43]. Wong HYF, Lam HYS, Fong AH, Leung ST, Chin TW, Lo CSY, Lui MM, Lee JCY, Chiu KW, Chung T, Lee EYP, Wan EYF, Hung FNI, Lam TPW, Kuo M, Ng MY. Frequency and distribution of chest radiographic findings in COVID-19 positive patients. *Radiology*, 2019: <https://doi.org/10.1148/radiol.2020201160>
- [44]. Conti B. Prostaglandin E2 that triggers fever is synthesized through an endocannabinoid-dependent pathway. *Temperature*, 2016; 3(1): 25-27.

- [45]. Buddhadasa R. Charaka Samhita, Sinhala translation, Chikithsa Sthana, Chapter 03, Vers 142-145. Colombo: Educational Department. 1960: p. 482.
- [46]. Buddhadasa R. Charaka Samhita, Sinhala translation, Chikithsa Sthana, Chapter 03, Vers 52. Colombo: Educational Department. 1960: p. 474.
- [47]. Panja AK, Chattopadhyaya A, Chaudhuri S. A comprehensive outlook of sannipata. *Ayu*, 2011; 32(2): 154-164.
- [48]. Bell DJ, Knipe H. COVID-19. *Radiopaedia*. [ONLINE] Accessed on 20.04.2020. Available at: <https://radiopaedia.org/articles/covid-19-3>
- [49]. Buddhadasa R. Charaka Samhita, Sinhala translation, Chikithsa Sthana, Chapter 03, Vers 155-161. Colombo: Educational Department. 1960: p. 485-490.
- [50]. Buddhadasa R. Charaka Samhita, Sinhala translation, Chikithsa Sthana, Chapter 03, Vers 324-328. Colombo: Educational Department. 1960: p. 1090.
- [51]. World Health Organization. Interim Guidance Document: Clinical Management of severe acute respiratory infections when novel coronavirus is suspected: What to do and what not to do. [ONLINE] Accessed on 20. 04. 2020. Available at: https://www.who.int/csr/disease/coronavirus_infections/InterimGuidance_ClinicalManagement_NovelCoronavirus_11Feb13_u.pdf
- [52]. Tiang Y, Rong L, Nian W, He Y. Review article: gastrointestinal features in COVID-19 and the possibility of faecal transmission. *Alimentary Pharmacology & Therapeutics*, 2020: <https://doi.org/10.1111/apt.15731>
- [53]. Easy Ayurveda. Charaka-shotha chikitsa 12th chapter. [ONLINE] Accessed on 20.04.2020. Available at: <https://www.easyayurveda.com/2015/09/26/charaka-shotha-chikitsa-12/>
- [54]. Bhashagratna KKL. Sushruta Samhita, Vol 06, Uttarasthana, Chapter 02, vers 5. [ONLINE] Available at: <https://www.wisdomlib.org/hinduism/book/sushruta-samhita-volume-6-uttara-tantra/d/doc142991.html>
- [55]. Raghuram YS. Krimigranthi, Janthugranthi Definition, Location, Symptoms, Treatment. [ONLINE] Available at: <https://www.easyayurveda.com/2018/06/20/krimigranthi-jantugranthi/>
- [56]. Dias MR, Guareschi BLV, Borges CR, Biazim DF, Casagrande D, Luz RA. B;epharitis: epidemiology, etiology, clinical presentations, treatment and evolution of our patients. *Rev Bras Oftalmol*, 2019; 78(5): 300-303.
- [57]. Bernades TF, Bonfioli AA. Blepharitis. *Semin Ophthalmol*, 2010; 25(3): 79-83.
- [58]. Liu J, Sheha H, Tseng SC. Pathogenic Role of Demodex mites in blepharitis. *Current Opinion in Allergy and Clinical Immunology*, 2010; 10(5): 505-510.
- [59]. Hewavithana T, Ranaweera KKDS, Tissera MHA, Yapa PAJ. Physico-chemical, chromatographic and spectrophotometric measurements in the standardization of Seetharama watee-a Sri Lankan herbo-mineral formulation. *International journal of pharmacy and pharmaceutical sciences*, 2012; 4(4): 575-578.
- [60]. Anpuchelvy S, Sritharan G. A study on the effects of a Kuppilai (Ennai) oil in the management of chronic wounds. *Salakya Sandipani*, Department of Shalya Shalakyaa, Gampaha Wickramarachchi Ayurveda Institute, University of Kelaniya, Sri Lanka, 2017; p. 66.
- [61]. Krishan WA. In-vitro study to evaluate the antibacterial activity of Buddharaja kalka with Makarandanvilapambul Anupana against *staphylococcus aureus*. *Salakya Sandipani*, Department of Shalya Shalakyaa, Gampaha Wickramarachchi Ayurveda Institute, University of Kelaniya, Sri Lanka, 2017; p. 67.
- [62]. Weerakoon WASS, Perera PK, Gunasekara D, Suresh TS. Evaluation of the in-vitro and in-vivo antioxidant potentials of Sudarshana powder. *Evidence based complementary and alternative medicine*, 2018; doi: 10.1155/2018/6743862.
- [63]. Amarasinghe APG. Scientific studies of a popular Sri Lankan indigenous therapeutic agent Rathakalka used in pediatric practice. *Planta Med*, 2009; 75-S-9: doi: 10.1055/s-2009-1216401.
- [64]. Ramesh P, Piyush G, Mohd T, Sanjay K. Herbal plants used for immunomodulatory action: a review. *International Journal of Research in Pharmacy and Science*, 2012; 2(3): 14-26.