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Overview of COVID-19 As Global Pandemic

Musmade Nirmala Ashok¹*, Kakade Swati Babasaheb¹, Musmade Deepak Sitaram², Shaikh Sabhafarin Hasin², Matsagar Aishwarya Rajendra², Aghade Karveer¹ 1.Matoshri Institute of Pharmacy, Vaijapur, India 2.Nanadkumar Shinde College of Pharmacy, Vaijapur, India

ABSTRACT

Beginning of the new decade was highlighted with the global outbreak of Coronavirus disease-19 (COVID-19). It is a kind of viral pneumonia which is caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), a new strain of Coronavirus. This outbreak of pneumonia with unknown etiology was thought to have originated from the Huanan seafood market and was reported firstly at Wuhan, in China. On 31st January 2020, the World Health Organization (WHO) announced that COVID-19 was listed as the Public Health Emergency of International Concern (PHEIC). The virus was named as COVID-19 on 11th February, 2020 by WHO. As it has affected the whole world, it was declared as global pandemic by WHO. SARS-CoV-2 is the betacoronavirus with presence of different proteins which helps in attachment, penetration, biosynthesis, maturation and release of newly synthesized virion particles in the host body and infect the host. COVID-19 is contagious and primarily spreads through the respiratory tract, by droplets, respiratory secretions, and direct contact. As no vaccine or drug molecule are available yet, breaking the chain, enhancing an individual's body immunity, identifying the infection early and timely medical care are the best ways to prevent COVID-19 infection. Along with Allopathy medicines, Ayurveda, Unani and Homeopathy medicines are used as add-ons to treat the disease. Thus, taking into consideration this global threat this review focuses on origin, morphology of SARS-CoV-2, pathogenesis, role of Ayurveda, Unani, Homeopathy and Allopathy in treatment of COVID-19 and the current scenario of vaccines against COVID-19.

Keywords: COVID-19, Pandemic, Ayurveda, Unani, Homeopathy, Allopathy.

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INTRODUCTION

Since past two decades coronavirus have caused epidemic diseases, namely Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory syndrome (MERS) and now recently it has been outbreaked as COVID-19¹. The first coronavirus that caused severe disease was SARS, was originated in Foshan, China, and resulted in the 2002-2003 SARS-CoV pandemic. The second coronavirus caused Middle East respiratory syndrome (MERS), which originated from the Arabian peninsula in 2012². Coronavirus disease 2019 (COVID-19) is a kind of viral pneumonia which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)³. In December 2019, novel coronavirus induced-pneumonia was reported as an outbreak of pneumonia from Wuhan in China, which rapidly spread worldwide. These patients most notably presented with clinical symptoms of dry cough, dyspnea, fever, and bilateral lung infiltrates on imaging. The causative agent was identified from throat swab samples conducted by the Chinese Centre for Disease Control and Prevention (CCDC) on 7th January 2020⁴. On 31st January 2020, the World Health Organization (WHO) announced that COVID-19 was listed as the Public Health Emergency of International Concern (PHEIC) and the virus was named as COVID-19 on 11th February, 2020 by WHO. The international virus classification commission named the novel coronavirus as Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2)^{5,6}. This outbreak was thought to have originated from the Hunan seafood market at Wuhan, in China. The patients presented with pneumonia of unknown etiology and had a history of travel to the seafood market. Gradually, the number of cases began to rise and few patients had no travel history to seafood market, indicating a possible human-to-human transmission ⁷. In this review we will focus on the overview of COVID-19 with respect to its origin, structure and pathogenesis of virus and treatment of COVID-19 with Ayurveda, Homeopathy, Unani and Allopathy.

Origin of COVID

The SARS-CoV-2 is a betacoronavirus. It belongs to the Nidovirales order, Coronaviridae family, Orthocoronavirinae subfamily and subgenus sarbecovirus ⁸. Coronaviruses are classified into four genera of CoVs: Alphacoronavirus (alphaCoV), Betacoronavirus (betaCoV), Deltacoronavirus (deltaCoV), and Gammacoronavirus (gammaCoV). Furthermore, the betaCoV genus divides into five sub-genera or lineages. Genomic characterization has shown that probably bats and rodents are the gene sources of alphaCoVs and betaCoVs. On the contrary, avian species seem to represent the gene sources of deltaCoVs and gammaCoVs ⁹. There are six human-susceptible virus, among which alphaCoVs HCoV-229E and HCoV-NL63, and betaCoVs HCoV-HKU1 and HCoV-OC43 have low.

Pathogenicity causes mild respiratory symptoms similar to a common cold, respectively. The other two known betaCoVs, SARS-CoV and MERS-CoV lead to severe and potentially fatal respiratory tract infections ¹⁰. It was found that the genome sequence of SARS-CoV-2 is 96.2% identical to a bat CoV RaTG13, whereas it shares 79.5% identity to SARS-CoV. Based on virus genome sequencing results and evolutionary analysis, bat has been suspected as natural host of virus origin, and SARS CoV- 2 might be transmitted from bats via unknown intermediate hosts to infect humans ¹¹.

Morphology of COVID-19

Coronaviruses are enveloped, pleomorphic or spherical particles, 150 to 160 nm in size. Prominent surface projections of up to 20 nm in length cover the entire virion surface, giving it crown like appearance ¹². As shown in Figure 1, the structure of CoV consists of positive single stranded RNA, nucleoprotein, capsid, matrix, and S-protein ¹³. Envelops covers a helical nucleocapsid of 6-8 nm in diameter. It consists of four types of structural proteins that is S protein, M protein, N protein, E protein and hemagglutinin – esterase (HE) protein.

S protein

It is also called as spike protein. It is type I membrane glycoprotein which constitutes of spikes or peplomers. It plays an important role in the initiation of viral infectivity. Spike glycoprotein shows high rate of mutation in corona virus ^{14, 15}.

M protein

This protein is found in abundance in membrane of the coronavirus and is also called as membrane protein. It spans the membrane bilayer three times, leaving a short NH₂-terminal domain outside the virus and a long -COOH terminal, inside the virion, as a cytoplasmic domain ¹⁶.

E protein

The envelope (E) protein has been detected as a minor structural component and most likely constitutes the smaller spikes that are observed on the virus particles in some electron micrographs of coronaviruses ¹⁷.

Hemagglutinin –esterase (HE) protein

This protein is the characteristic feature of the betacoronvirus. This protein helps to bind sialic acid on the host cell surface glycoproteins. It helps to enhance entry and pathogenesis of coronavirus ¹⁸.

Nucleocapsid (N) protein

N-protein is a phosphoprotein which constitute of nucleocapsid protein of a virus. This protein binds to virion RNA and helps in viral RNA synthesis ¹⁹.

PATHOGENESIS AND SYMPTOMS OF COVID-19

Angiotensin converting enzyme-2 (ACE2) is main site for binding of SARS-CoV-2^{7, 20, 21}. As shown in Figure 2, life cycle of virus within the host cell consists of five major steps. Attachment, penetration, biosynthesis, maturation and release are the steps of pathogenesis of SARS-CoV-2 within the host cell.

Attachment is the important step in which S protein of virus binds to host receptors ACE-2 or type-2-transmembrane serine protease (TMPRSS2) and penetrates inside the host cell through endocytosis or membrane fusion mechanism ²². On complete penetration of virus inside the host cell, viral contents are released and the viral RNA attacks the host cell nucleus for replication. Viral mRNA undergoes replication and synthesize new viral proteins. These newly synthesized viral proteins are assembled in host cell. This step is called as maturation stage which results in formation of new viruses. These new virus are then released outside the host cell which again binds to another host cell and the proliferation of virus continues ^{23, 24}. As an emerging acute respiratory infectious disease, COVID-19 primarily spreads through the respiratory tract, by droplets, respiratory secretions, and direct contact (Figure 3) ²⁵.

COVID-19 is contagious during the latency period and its incubation period is 1-14 days ²⁶. It is highly transmissible in humans, especially in the elderly and people with underlying diseases. The median age of patients is 47–59 years and 41.9–45.7% of patients were females ²⁷. A COVID-19 patient shows major symptoms such as fever, sore throat, runny nose and cough (Figure 3) ²⁸. Most adults or children with SARS-CoV-2 infection presented with mild flu-like symptoms and a few patients are in critical condition and rapidly develop acute respiratory distress syndrome, respiratory failure, multiple organ failure, even deaths ²⁹.

TREATMENT OF COVID-19

COVID-19 pandemic is unique and unprecedented in several aspects and has challenged health care systems across the globe. Till date, no medicinal system of India or therapy has demonstrated promising results in either preventing the disease or improving its prognosis to prevent this infection. Breaking the chain, enhancing an individual's body immunity, identifying the infection early and timely medical care are the best ways to prevent COVID -19 infection ³⁰. Different traditional like Ayurveda, Unani, and homeopathy are used as prophylactic against COVID-19. Along with the investigation on virology of SARS-CoV-2, understanding the fundamental physiological and immunological processes underlying the clinical manifestations of COVID-19 is vital for the identification and rational design of effective therapies. Until development of potential vaccine, it is necessary to build up strong immunity to protect oneself from COVID-19 ³¹.

Role of Ayurveda in COVID-19

The traditional practice helps to improve psychological quality of life, and reducing the risk of infection. Ayurveda is one of the traditional medicine systems of India which has enough potential and possibilities to be employed both for the prevention and an adjunct treatment option for COVID-19³². The Ayurveda pays main attention on building strength of mind and body to cope with various stressors, including infection. The classic Ayurveda text *"Charaka Samhita"* had explained about epidemic management and defines immunity as the ability to preventing and arresting the progression of disease for maintaining homeostasis. In Ayurveda several treatment options are available for enhancing immunity against respiratory illnesses; these include certain immunomodulators (known as Rasayana), local and systemic interventions ³³.

As per Ayurveda, the COVID-19 pandemic is due to *Vikruti* (Contamination) of *Vayu* and *Dosha*. COVID-19 infection may be considered as *Upsargika Roga* (communicable disease), which can be included under *Abhishangaja Jwara* and it is one among four types of *Agantuja Jwara* (fever caused by external factors may be like virus etc.) ³⁴. As disease progresses, it impairs the efficiency of the *Doshas* and gets converted to *Nija Vyadhi* (endogenous diseases). It may resemble to *Vata-Kaphaja Sannipataja Jwara* with the symptoms like feeling of cold, cough, anorexia, drowsiness, thirst, burning sensation and pain. Further, it may be complicated by symptoms like dysponea and with high fatality rate which occurs in advanced stage of COVID-19. According to Charak Samhita, *Rasayana* and *Panchakarmas* are the main management principles in this condition ³⁵. In India, several initiatives have been taken to utilize the vast potential of Ayurveda in this pandemic. The Ministry of Ayush, a nodal Ministry of Complementary and Alternative Medicine, has released a set of guidelines for boosting immunity and measures for self-care by using Ayurvedic principles ³⁶.

Local prophylaxis measures such as herbal decoctions, consumptions of hot water, gargling with medicated water, and steam inhalation are described in Ayurveda for respiratory illnesses in mild cases ³⁷. Diet, sleep, mental relaxation, lifestyle behavior, and Yoga are the non- pharmacological parameters which help to maintain the overall health. Yoga plays a crucial role in improving lung health and exercise tolerance ^{38, 39}. Pranayama improves the lung function ⁴⁰ and meditation helps to reduce inflammation markers and influence markers of virus-specific immune response ⁴¹.

Yoga including meditation could be a simple and useful home-based practice for the prevention and post-recovery management of COVID-19. The *Rasayanas* helps to enhance the immunity and can be used in COVID-19 pandemic. The different *Rasayanas* includes *Chyavanprash, Amlaki Rasayana, Kushmanda Rasayana, Agastya Haritaki, Chitraka Haritaki,* and *Ardhraka Khanda* and specifically used in *Shwasa* and *Kasa* diseases. These *Rasayanas* are mainly administered daily morning with milk except *Amlaki Rasayana*^{42, 43}. The common drugs or herbs, which are used regularly in food are indicated in *Jwara, Kasa* and *Shwasa* have antiviral effects as well as immunomodulatory effect. These herbs are *Haridra* (turmeric)⁴⁴, *Tulasi* (holy basil)^{45, 46}, *Ardrak* (ginger)⁴⁷, *Nagaveli* (betel leaf), *Yastimadhu* (licorice), *Pippali* (long pepper), *Guduchi* (giloy), Parijata (night-flowering coral jasmine), *Lasuna* (garlic)^{42, 48, 49}.

Role of Allopathy in COVID-19

Allpothaic treatment focus on repurposing older molecules in COVID- 19, as their safety profile has already been documented ⁵⁰. It includes like protease inhibitors (PIs), antiviral drugs, RNA polymerase inhibitors, immunomodulators and anti-inflammatory drugs, membrane fusion inhibitors and inhibitors of ACE2 receptor. Lopinavir and ritonavir are the protease inhibitors used to treat infection with human immunodeficiency virus (HIV). It has reported that betacoronavirus viral loads of a COVID-19 patient in Korea significantly decreased after lopinavir/ ritonavir treatment ⁵¹. 3CLpro plays an important role in processing viral polyproteins ^{52, 53}. PIs effectively inhibit the 3CLpro enzyme, thus posing a possibly potent therapeutic agent against SARSCoV-2 infection. Remdesivir is an adenosine analogue with broad spectrum antiviral drug which has the potential to outcompete the proofreading ability of coronavirus exonuclease, and carries a high genetic resistance barrier and Wang et al. confirmed its in-vitro efficacy against SARS-CoV-2⁵⁴, ^{55, 56}. Favipiravir is a nucleoside analogue inhibiting the RNA polymerase and is effective against a broad range of viruses, including positive-sense single-stranded RNA viruses ⁵⁷. Ribavirin is a guanosine analogue that inhibits inosine monophosphate dehydrogenase in combination with either lopinavir/ritonavir or Interferon alpha were used in SARS epidemic and these combinations are currently recommended by the China National Practice Guidelines for the treatment of severe COVID-19⁵⁷.

Chloroquine is an antimalarial drug which inhibits pH-dependent steps of the replication of several viruses. It showed potent effect on SARS-CoV infection. It interferes with the glycosylation of cellular receptors of SARS-CoV and functioned at both entry and at post-entry stages of the COVID-19 infection in Vero E6 cells ⁵⁸. An in-vitro study by Caly *et al.* showed that ivermectin, a broad-spectrum antiparasitic agent, was able to reduce viral replication at 48 h in SARS-CoV-2-infected Vero-hSLAM cells ⁵⁹.

Anti-viral medicines like oseltamivir, ganciclovir, ribavirin, favipiravir, arbidol, remdesivir and galidesivir are being investigated for COVID-19 treatment ⁶⁰⁻⁶³. According to Wang et. al., findings reveal that remdesivir and chloroquine are highly effective in the control of SARS-CoV-2

infection in-vitro and was suggested to use this combination in patients suffering from novel coronavirus disease ⁵⁶.

Role of Unani Medicines 64-67

The Unani medicines are plant-based medicines which are nontoxic and have no side effects. The different parts of the various plants are well known for a long time for their anti-viral activities like Glycyrrhiza glabra, Allium cepa, Allium sativum, Ocimum sanctum, Ocimum tenuiflorum, Piper nigrum, Cinnamomum verum, Daucus maritimus, Curcuma longa, etc. An aqueous extract of these plants along with lemon juice and honey was found to be effective for flu and common cold virus infections. On January 29, 2020, the Government of India issued an advisory based on Indian traditional medicine practices Ayurveda, Homeopathy and Unani, New Delhi. The advisory includes the ways of preventive management and described a list of some Unani medicines. It includes:

- 1. Sharbat Unnab 10-20ml twice a day
- 2. Tiryaq Arba 3-5g twice a day
- 3. Tiryaq Nazla 5g twice a day
- 4. Khamira Marwareed 3-5g once a day
- 5. Massage on scalp and chest with Roghan Baboona/ Roghan Mom/ Kafoori Balm
- 6. Apply Roghan Banafsha gently in the nostrils
- 7. Take Arq Ajeeb 4-8 drops in fresh water and use four times a day
- 8. In case of fever, take Habb-e-Ikseer Bukhar 2 pills with lukewarm water twice daily.
- 9. Sharbat Nazla 10ml mixed in 100ml of lukewarm water twice daily.
- 10. Qurs-e-Suaal 2 tablets to be chewed twice daily.
- 11. Arq extracted from any single unani drugs like *Chiraita, Kasni, Afsanteen, Neem Bark* along with Sharbat Khaksi is very useful.
- 12. Decoction of single unani drug like Behidana, Unnab, Sapistan, Darchini, Banafsha.

Role of Homeopathy

The preventive aspect of Homoeopathy is well known, and historically. It has been used during the epidemics of Cholera, Chikungunya, Dengue Fever, Spanish Influenza, Yellow fever, Scarlet fever, Diphtheria, Typhoid etc. In homeopathy, treatment mainly depends on Genus epidemicus. The Genus epidemicus is identified through observation of several cases of an epidemic disease, and analyzing the symptomatology of those cases for the most indicated medicine. This medicine is the preventive medicine for the ongoing epidemic of that disease. With regard to the positive results from the prophylactic homoeopathic medicine during epidemic outbreaks of various

diseases during recent past, the Scientific Advisory Board of our Council advised to find out possible genus epidemicus for COVID-19, in the meeting held on 28 January 2020. The Directorate of AYUSH, New Delhi, India suggested taking 4 pills of Arsenic Album-30 medicine once daily in empty stomach for 3 days. Arsenic Album-30 is highly diluted arsenic trioxide and work as homeopathic prophylaxis⁶⁸.

Current scenario of Vaccines against COVID-19

To cope up with the pandemic of COVID-19, the researchers all over the world are working around the clock to find a vaccine against SARS-CoV-2. To date, just one coronavirus vaccine has been approved. Sputnik V – formerly known as Gam-COVID-Vac and developed by the Gamaleya Research Institute in Moscow – was approved by the Ministry of Health of the Russian Federation on 11 August. Till date (20 August, 2020), 42 candidates are under clinical trials, out of which Inactivated vaccine of Sinopharm, CoronaVac of Sinovac, mRNA-1273 of Moderna and Ad5-nCoV of CanSinoBiologics are in phase 3 clinical trials ^{69,70}.

CONCLUSION

Coronavirus disease 2019 (COVID-19) is a kind of viral pneumonia which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which was reported as an outbreak of pneumonia from Wuhan in China, which rapidly spread worldwide and was declared as pandemic by WHO. The patients show flu-like symptoms with high fever and breathing problems. The disease due to SARS-CoV-2 was named as COVID-19.Till date, there is no promising treatment for this disease. However, prevention and management are the best options. Breaking the chain, enhancing an individual's body immunity, identifying the infection early and timely medical care are the best ways to prevent COVID-19 infection. Ayurveda, Unani, Homeopathy and Allopathy play an important role in treatment of COVID-19. Ayurveda mainly focuses on the use of different drugs showing antiviral and immune modulation properties. Arsenic album 30 as prophylactic homoeopathic medicine. Allopathic medicines focus on repurposing of the old medicines like antiviral drugs, immunomodulatory, protease inhibitors and RNA polymerase inhibitors. However, whole world is facing a challenge in dealing with a new coronavirus infection that has just emerged in humans. There is no need to be panic and proper prevention and management are essential to combat this disease. It is also essential to put collective efforts globally not only to invent the proper therapeutics and potential vaccine but also to make it available for all. This will help to settle this global Covid-19 issue.

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