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Different aspects of the current pandemic situation of COVID-19- a comprehensive review

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Abstract: An unusual episode of pneumonia happened in Hubei Province, Wuhan City(China) in December 2019.A novel coronavirus was recognized as the causative agent. The situation was declared a pandemic by WHO (World Health Organisation) and the disease was named as COVID-19. The outbreak progresses faster than SARS and MERS coronaviruses but has less mortality than the two precursors. COVID-19 cases continue to intensify, despite meticulous global containment and quarantine efforts. Gathered from the evidences currently published, this review deliberately summarizes the findings of COVID-19 disease transmission, pathogenesis, manifestations, analysis, treatment, and counteraction.

Keywords: COVID-19, transmission, analysis, treatment

1. Introduction

Coronaviruses are enclosed retroviruses that are commonly distributed among humans, various vertebrates, and birds, causing respiratory, gastric, hepatic, and neurological diseases [1, 2]. It is estimated that six coronavirus species cause human diseases. The four viruses that are predominant and normally cause common cold symptoms in immunologically competent individuals are 229E, OC43, NL63, and HKU1[3]. Severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) are two other zoonotic strains that have been linked to sometimes fatal illness[4]. In Guangdong Province, China, SARS-CoV induced severe acute respiratory syndrome outbreaks in 2002 and 2003[5-7]. In 2012, MERS-CoV was the pathogen responsible in the Middle East for extreme respiratory infection flare-ups[8].

Several patients with pneumonia of obscure reason were revealed by a few local health offices at the end of December 2019whichwas epidemiologically linked to a seafood wholesale market in Hubei Province, Wuhan, China, [9]. On 31 December 2019, the Chinese Center for Disease Control and Prevention (China

CDC) dispatched a quick response team to accompany the provincial health authorities of Hubei and execute an epidemiological and pathophysiological investigation. The 2019-nCoV, a novel beta-coronavirus associated with the sarbecovirus subgenus of the Coronaviridae family, is recognized as the primary cause of Wuhan viral pneumonia[10], which was later named SARS-CoV-2 and WHO named the disease COVID-19.

In this review we have discussed a comprehensive guide of COVID-19; its manifestations, transmission, identification, treatment, and anticipation.

2. Symptoms

Symptoms of infection with COVID-19 can occur within 2 days to 2 weeks of exposure to the virus, with an incubation time of approximately 5.2 days. [11]. This period is subject to the patient's age and position of the immune system ofthe patient. Patients > 70-years old develop symptoms in the early days thanthose who areyounger than 70 [12]. Fever, cough, and weakness are the most frequent signs at the onset of COVID-19 disease, although other symptoms include salivation, neuralgia, haemoptysis, indigestion, and breathlessness(figure 1) [13, 14, 15]. While there are certain symptotic parallels between COVID-19 and existing beta-coronaviruses on chest CT scans, like fever, chest infection, shortness of breath, and bilateral ground-glass opacities[14], COVID-19, however, revealed certain distinctive clinical characteristics that involve the targeting of the lower aviation path as evident from signs of the upper airway such as nasal discharge, sniffling, and sore throat [16,17]. In addition, some cases display infiltration of the upper lung lobe that is consistent with increasing dyspnea and hypoxemia, based on the findings of lung x-rays [18]. In comparison, a low proportion of MERS-CoV or SARS-CoV patients experienced related GI (Gastro-intestinal) conditions, while patients with COVID-19 developed GI symptoms such as diarrhoea[16.17]. Aside from these, new symptoms are also observed i.e. the loss of taste (ageusia) and smell (anosmia) in COVID-19 patients [19,20].

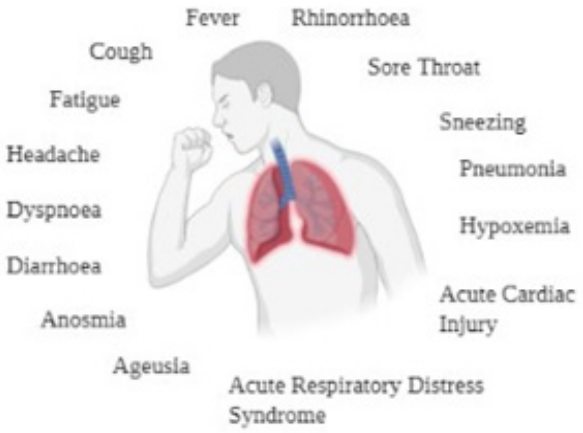

Figure 1. Symptoms of COVID-19

3. Epidemiology and Pathogenesis

The epidemic originally erupted in Wuhan, China, in December 2019. There is still no confirmation that the birthplace of SARS-CoV-2 emerged in the fish market, although it is related to the same. A few experiments showed that the possible store of SARS-CoV-2 maybe bats[21, 22]. Preferably, bats are the natural source of a wide assortment of CoVs, including SARS-CoV-like and MERS-CoV-like viruses [23,24,25]. Upon infection genome sequencing, the COVID-19 was investigated all through the genome to Bat CoV RaTG13 and indicated 96.2 percent oftotal genome sequence character [26], recommending that bat CoV and human SARS-CoV-2 may have a similar predecessor [27].

Though the pathogenesis of COVID-19 is not clearly understood, the similar mechanisms of SARS-CoV and MERS-CoV facilitate the pathogenesis recognition of SARS-CoV-2 infection,as depicted in figure 2. The spike

proteins (S proteins) of coronavirus have been described as the contributing factor of virus entry into host cells [28].These spike glycoproteins stick to its cellular receptor,ACE2 (angiotensin-converting enzyme 2), which is present in pulmonary, intestinal, kidney, and blood vessel epithelial cells[29]. Immediate membrane fusion between the virus and the plasma membrane of the host cell initiates the entry of the virus into cells. [30].The RNA genome of the virus is released into the cytoplasm when the virus reaches the cells and is translated into two polyproteins and structural proteins, and then the viral genomic replication begins [31]. The freshly formed envelope glycoproteins are forced into the endoplasmic reticulum or Golgi membrane and the combination of nucleocapsid protein and genomic RNA shapes the nucleocapsid. Viral particles subsequently expand into the intermediate compartment of the endoplasmic reticulum-Golgi (ERGIC). Finally, to unleash the virus, the vesicles carrying the virus particles fuse with the plasma membrane. [28].

4. Who are at risk?

While respiratory symptoms dominate the clinical presentations of COVID-19, patients with coronary disease, hypertension, or diabetes are at greater risk of serious COVID-19 infection and may have an elevated risk of death[32].

Human pathogenic coronaviruses (SARS-CoV and SARS-CoV-2) bind to their target cellsvia angiotensin-converting enzyme 2 (ACE2)[33]. In the cardiovascular and immune systems, ACE2 is a membrane-bound aminopeptidase that plays an invaluable role[34]. Heart activity and the progression of hypertension and diabetes mellitus are linked with ACE2. ACE inhibitors and ARBs (Angiotensin II receptor blockers)

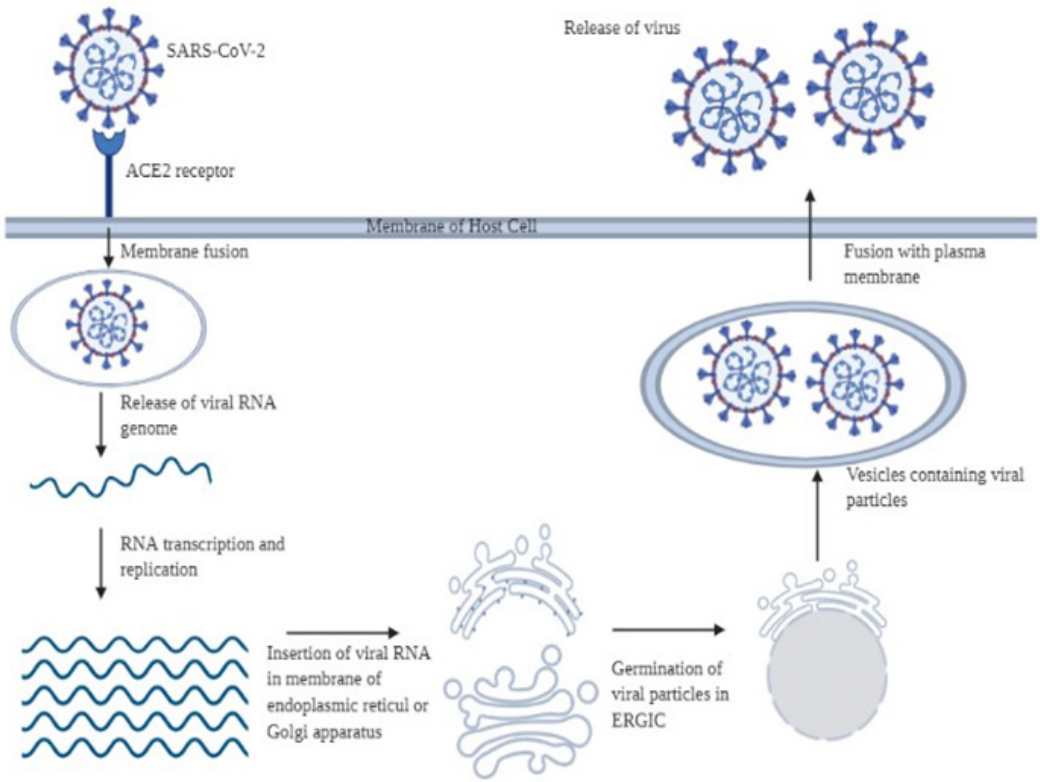

Figure 2. Schematic representation of pathogenesis of SARS-CoV-2.

are used to treat hypertension and diabetes, leading to an upregulation of ACE2[35]. Thiazolidinediones and ibuprofen can also increase ACE2. The increased expression of ACE2 would thus promote COVID-19 infection. It is also hypothesized that extreme and lethal COVID-19 can develop by treatment of diabetes and hypertension with ACE2-stimulating medicines.

5. Transmissionpath of SARS-CoV-2

It is possible to communicate the novel CoV in humans through respiratory droplets. The pulmonary system, though, is presumably not the only direction of transmission. The virus may be spread to the eyes, mouth, or nose by direct or indirect exposure with mucous membranes [36, 37]. Additionally, in an almost closed atmosphere with continuous contact, there is a risk of aerosol transfer. Besides, certain symptoms of the gastrointestinal tract, including diarrhea, fatigue, and vomiting, have been documented by certain COVID-19 patients [38, 39]. Recent research has shown that the digestive tract, apart from the respiratory path, is also a possible route for COVID infection. [40].

6. Diagnosis

To monitor the outbreak of COVID-19, rapid and accurate detection of SARS-CoV-2 is important. A significant tool of laboratory interpretation is nucleic acid detection. Reverse transcription quantitative Polymerase Chain Reaction (RT-qPCR) is a molecular biological analytical tool that relies on nucleic acid sequences. The full sequences of the SARS-CoV-2 genome are available at GenBank. A sampling of nasopharyngeal and oropharyngeal swabs, stools, mucus, or blood tested by RT-qPCR or viral genome sequencing will then diagnose SARS-CoV-2 nucleic acid[41]. However, the handling of these types of specimens by healthcare professionals requires close communication with patients, posing a chance of exposure to the infection to healthcare workers. In addition, the collection of nasopharyngeal or oropharyngeal specimens can cause bleeding,particularly in patients with thrombocytopenia[42]. Significantly, To et al. found that the virus could be successfully identified in infected patients' saliva specimens[43], indicating that saliva is a viable non-intrusive specimen type for COVID-19 patient detection, surveillance, and infection control.

In clinical practice, chest radiograph / CT is also a major procedure for COVID-19 diagnosis. Most cases of COVID-19 have comparable characteristics on CT scans, including bilateral distribution of irregular shadows and opacity of ground glass.The CT scans can be correctly analyzed and are diagnostically very useful [44].

7. Treatments

COVID-19 general care requires bed rest, proper energy consumption, and control of vital indicators such as heart rate, blood pressure, levels of oxygen, etc. Critical patients need to be brought to hospitals as early as possible. Other confirmed/suspected cases should be quarantined and separated at home.

7.1. Antiviral therapy

7.1.1. Interferon-alpha (IFNα)

By direct interaction with virus replication and fostering immune responses, IFNα suppresses viral infection. In vitro investigations have shown that IFNα effectively inhibits SARS-CoV replication [45, 46]. Cynomolgus monkeys have also been reported to be rescued from SARS-CoV infection by treatment with IFNα[47]. A clinical trial furthermore confirmed

the therapeutic value of IFNαfor patients with SARS[48]. IFNα should also be considered a possible drug candidate for treatment with COVID-19.

7.1.2. Lopinavir and ritonavir (Kaletra)

Lopinavir and ritonavir are protease inhibitorsthatare used in the treatment of human immunodeficiency virus (HIV) [49,50]. Some reported molecular models indicate that lopinavir and ritonavir can bind to SARS-CoV-2 protease endopeptidase C30 [51]. This indicates that, by inhibiting SARS-CoV-2 protein synthesis, this medication can exert an antiviral effect. Furthermore, these antiviral drugs havebeen shown beneficial in serious patients with SARS and MERS[52,53,54]. Hence,it may have a positive effect on COVID-19 patients, since SARS-CoV-2 is identical to these two viruses. To verify this possibility, further investigations are required.

7.1.3. Ribavirin

Ribavirin is an analogue of synthetic guanosine with broad antiviral efficacy. It interferes with the synthesis of viral RNA and has been extensively used to treat patients with SARS infection since the 2003 SARS outbreak in Hong Kong [55,56,57] Thus, ribavirin may also be a treatment choice for patients with COVID-19.

7.1.4. Chloroquine and hydroxychloroquine

Aminoquinolines, which have been used to combat malaria and autoimmune disorders for more than 50 years, are chloroquine and hydroxychloroquine. These two drugs are poor diprotic bases and are capable of raising endosome pH, preventing viral cell fusion[58]. Multiple clinical trials are being performed in China to determine the effectiveness and safety of chloroquine and hydroxychloroquine in COVID-19, one of which has shown that chloroquine is superior,encouraging virus-negative conversion and shortening the duration of the disease[59]. The preliminary analysis in France, meanwhile, tested the effectiveness of hydroxychloroquine in COVID-19 patients [60].

7.1.5. Remdesivir

Remdesivir, an inhibitor of viral RNA, has been reported to inhibit in vivo SARS-CoV and MERS-CoV [61,62]. In the recent past, an in vitro investigation found that remdesivir has firmly blocked low-micromolar SARS-CoV-2 infection and has demonstrated high selectivity [63]. While it has some advantages in the treatment of COVID-19, in order to assess its effectiveness and protection, randomized controlled trials are still needed.

7.1.6. Favipiravir

Favipiravir is a derivative of pyrazine carboxamide (6-fluoro-3-hydroxy-2-pyrazinecarboxamide) and a wide-spectrum antiviral medication approved for influenza treatment in Japan [64].Favipiravir competes with purine nucleosides and, by adding into the RNA virus, interferes with viral replication and thereby effectively inhibits the RNA-dependent RNA polymerase (RdRp) of RNA viruses[65].

7.2. Immunotherapy

7.2.1. Convalescent plasma therapy

In the recovering plasma of healed patients, antiviral antibodies are detected which can cure patients with viral infections. Infectious diseases such as poliomyelitis, influenza A (H5N1), and Ebola were used extensively with invasive plasma treatment [66,67,68]. In comparison, passive immunization can also be done with convalescent plasma in SARS-CoV patients. It has been documented that a few patients

with SARS-CoV-infected plasma in Taiwan and Hong Kong received early care with some clinical benefits, including a decrease in plasma viral loads from approximately 105 copies / mL to undetectable in 24 hours after transfusion [69,70,71]. Theoretically, convalescent plasma may be a potential solution in COVID-19 treatment.

7.2.2. Monoclonal antibodies

Reduction of the outbreak of SARS-CoV-2 will depend on monoclonal antibody innovations. Different viable monoclonal antibodies to prevent the virus from accessing the host cells were identified previously for the SARS-CoV spike protein[72, 73, 74]. The spike protein receptor-binding domain (RBD) is the primary target of neutralizing monoclonal anticorps [75]. The CR3014 and CR3022 SARS-CoV neutralizing monoclonal antibodies were found to bind the RBD of SARS-CoV non-competitively and synergistically neutralized the virus [76]. The ongoing research has shown CR3022 to be powerful in combination with SARS-CoV-2 RBD [77]. In comparison, the CR3014 epitope does not coincide with the SARS-CoV-2 RBD binding site of the ACE2 [76]. Thus, CR 3022 may be a therapeutically promising candidate for the treatment of COVID-19 pneumonia, alone or with other neutralized monoclonal antibodies.

8. Preventive measures

No unique antiviral therapy has been reported to date as being successful against COVID-19. Proper indicative management and preventive care have been prescribed for patients afflicted with COVID-19 [11,77]. A variety of steps to mitigate nosocomial infection have been recommended, including awareness preparation for prevention and monitoring, segregation, disinfection, graded safety at differing degrees in the contamination regions, and protection of reported cases[78, 79].

There are no immunizations forestalling COVID-19 for the general public as of now. The best anticipation is to prevent exposure to the virus. Airborne precautions and other protective strategies have been addressed and recommended for counteraction. The following are infection prevention and control (IPC) steps that may minimize the risk of exposure[77]:

- Facial mask utilization;
- Cover tissue while coughing and sneezing and then cut them securely (or use a flexed elbow to cover the cough or sneeze, if there are no tissues available);
- Frequent washing of hands with soap or hand sanitizer disinfection containing a minimum of 60% alcohol;
- Prevent communication with infectious persons and establish as far as possible an acceptable distance;
- Refrain from touching the eyes, nose, and mouthwith unwashed hands.

The WHO has also published extensive guidelines on the use of face masks[80]. Healthcare staff is advised in this document to use particulate breathers, such as licensed N95 or FFP2, and people with coughing symptoms are recommended to use medical masks correctly according to infection control recommendations both in hospitals and in home care. Careful application and disposal of masks is also very importantotherwise the chance of transmission will increase[80].

In addition to the social prevention initiatives, masks, and hand washing, the enhancement of the body's natural protection (immunity) mechanism plays a major role in ensuring optimal fitness. Prevention, as we all know, is better than cure and it would be good to take proactive steps to improve our immunity. The following self-care recommendations

for improving immunity with specific regard to respiratory wellbeing are advised by the AYUSH Ministry [81].

- Drinking warm water and practicing yogasana/Pranayam is recommended.
- Spices like Haldi (Turmeric), Jeera (Cumin), Dhaniya (Coriander), and Lahsun (Garlic) should be used in cooking.
- Decoction (Kadha) made from Tulsi (Basil) [82, 83], Dalchini (Cinnamon) [84], Kalimirch (Black Pepper) [85], Shunthi (Dry Ginger) [86] and Munakka (Raisin) [87] should be consumed.
- Golden milk (turmeric in milk) is also a great immunity booster [88] and is highly recommended.
- Sesame oil/ coconut oil or ghee should be applied in both nostrils.
- Steam inhalation must be performed often.
- Clove should be taken in case of cough or throat discomfort [89].

We need effective preventative, promotive, curative and rehabilitative approaches to manage the onslaught of COVID-19. Modern medicine has very little to offer to manage COVID-19 patients. Integrating Ayurveda and Yogawith modern medicine will offer a novel and effective way to manage the current ongoing pandemic of COVID-19 [90,91].

The coming winter season can be more challenging as there are chances of intensification of viral circulation as observed with the return of cold season in some countries[92].At this stage, only non-pharmaceutical interventions, such as social distancing, patient isolation, face masks and hand hygiene, have proven effective in controlling the circulation of the virus and should therefore be strictly enforced.

9. Conclusion

In conclusion, COVID-19 has become an extremely contagious disease. Its primary clinical signs are close to those of other SARS infections: fever, cough, and fatigue. It is indeed a potentially deadly virus that can be spread through suspended particles and direct contact. Some instances are life-threatening; especially those with heart, diabetic, and pulmonary conditions in particular. COVID-19 presents a significant danger to public safety and its well-being. The key concern is monitoring the transmission of the disease and reducing mortality as quickly as possible. The virus's precise mechanism remains unclear, and no specific antiviral drugs have been produced. It is currently necessary to monitor the source of infection, to break off the path of dissemination, and to use available medicines and resources to proactively control the development of the disease. We must also aim to produce specific medicines, support vaccine research, and development, and reduce morbidity and mortality of COVID-19 in order to ensure the wellbeing of the population.

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Conflict of interest

The authors declare no conflict of interest.

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