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A Review on COVID-19: A Global and Sri Lanka Perspective

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ABSTRACT:- An outbreak of COVID-19 sparked initially in Wuhan city which is the capital of Hubei province in China and was declared as a public health emergency of international concern in late January, 2020 and then as a pandemic on 11th of March 2020. According to the WHO, by 25th April, 2020, 2,724,809 confirmed cases and 187,847 deaths were reported globally revealing its highly contagious nature and the risk of high mortality and morbidity all over the world. Two potential viruses; bat coronavirus (BatCoV RaTG13) found in *Rhinolophus affinis* and the beta corona virus found in Pangolins are known to be parental viruses of COVID-19 with their high sequence similarities in the complete genome and the receptor binding domain with that of SARS-CoV-2 respectively. Common clinical symptoms include fever, dry cough, dyspnea, myalgia, headache, tiredness and sore throat. The availability of latest molecular and radiological diagnostic measures have provided remarkable opportunities in the early detection of the disease, however, neither validated antiviral drugs nor vaccines have so far been developed with a verified efficacy. This review summarizes the origin, transmission, clinical characteristics, virulence, detection, treatment, prevention and control measures of the disease and the notable controlling measures which have been implemented in Sri Lanka to strictly prevent the COVID-19 progression and in turn restore the ordinary life style and the economy of the country.

Key words: Coronavirus, prevention & control, transmission, virulence

I. INTRODUCTION

Coronaviruses are positive stranded RNA viruses [1] which belong to Coronaviridae family in Nidovirales order [2] and sarbecovirus subgenus [3]. It contains a larger viral genome as the nucleic material, size ranging from 27-33kbs [1]. They contain crown shaped spike proteins on their outer membrane surfaces and therefore, are named "coronavirus". At the beginning of the 21st century, highly contagious and pathogenic coronaviruses appeared in humans and animals causing respiratory and intestinal infections in China and Saudi Arabia [4] and later spreading worldwide. In 2003, Chinese people in Guangdong province were identified as infected with Severe Acute Respiratory Syndrome (SARS) and later it was named as SARS-CoV [1, 5]. Initially, it emerged in China and later spread rapidly over the world affecting more than 8000 people in 25 countries and causing 774 deaths at the end of the outbreak [5]. In 2012, Saudi Arabians were diagnosed with another coronavirus called Middle East Respiratory Syndrome Coronavirus (MERS-CoV) [6]. It first originated in Middle East and then spread to Europe, Asia and North America as well [7], infecting more than 2428 people and causing 838 deaths according to the world health organization [8]. These coronaviruses have caused pneumonic changes in the lungs and diffuse alveolar damage producing acute respiratory distress syndromes (ARDS) [5, 9].

Recently, an outbreak of a novel coronavirus infection was experienced by Chinese population in Wuhan city. It was assumed to have originated from Hunan seafood market in Wuhan city in which a number of live animals were sold to be consumed as food [10]. There is also another speculation that the virus originated in research laboratories in America or Europe [11]. Initially, the virus was named as 2019 novel coronavirus (2019-nCov) by Chinese researchers and subsequently the name was changed as SARS-CoV-2 by the

International Committee on Taxonomy of Viruses (ICTV) and the disease it caused was named as COVID-19 by the world health organization [12, 13]. Earlier it was identified that the people who visited the sea food market had been infected with the virus. However, later investigations have reported of infected people who had no prior history of visiting the sea food market, indicating the possibility of transmission of the virus among human beings. Consequently, the virus spread rapidly beyond China in a short period of time causing epidemics in many countries worldwide and was declared as an international public health emergency by World Health Organization (WHO) on 30th January, 2020. This epidemic of COVID-19 was later reconsidered as a pandemic by the WHO within 42 days of the public health emergency (11th March, 2020) [14]. As of 25th April, 2020, 2,724,809 confirmed cases and 187,847 deaths in 213 countries all over the world were reported [15].

II. ORIGIN AND TRANSMISSION

Knowledge about the origin and transmission is very crucial to prevent and control the infection [2]. Two viruses are known to be acting as parental viruses of SARS-CoV-2, in spite of their varying overall genome sequence and amino acid sequences in the receptor binding domains. One is the bat coronavirus (BatCoV RaTG13) found in *Rhinolophusaffinis* from Yunan Province, which has shown 96.2% similar overall genome sequence with SARS-CoV-2 [16] and 89% similarity in amino acid sequence in receptor binding domain with that of the SARS-CoV-2 [13]. The other one is a beta corona virus that was found in Pangolins [17] that has 90% similar nucleotide sequence with SARS-CoV-2 and 97.4% identity in amino acid sequence in receptor binding domain with that of SARS-CoV-2. Due to this divergent sequences, immediate hosts and the reservoirs are not yet being concluded [13].

When the COVID-19 is considered, transmission of infection is occurring exponentially all over the world compared to that of the SARS and MERS outbreaks [7]. The virus is known to be transmitted from an infected person to another person via respiratory droplets through coughing, sneezing or with close contact [18]. In addition to the transmission via respiratory droplets and close contact, evidence for fecal-oral transmission is also available [19]. This evidence regarding fecal-oral transmission is supported by gastrointestinal symptoms of the COVID-19 disease and the isolation of the virus in the fecal samples of the confirmed patients [13].

III. CLINICAL CHARACTERISTICS

The most frequent clinical features that have been observed in the infected patients were fever, dry cough, dyspnoea and myalgia [18, 20, 21]. Additionally, lymphopenia and prolong prothrombin time was also noted [18, 20]. Clinical symptoms can vary according to the stage of the infection- mild, moderate, severe and critical [14]. Apart from the general clinical characteristics seen in the patients, COVID-19 associated myocardial infarction also should be taken into account. Multiple mechanisms which could predispose to this are shown by Li et al., (2020) [22]. Angiotensin converting enzyme 2 (ACE2), is an enzyme that attaches to the outer cell membrane in various human cells including cells in oral and nasal mucosa, lung, stomach, small intestines, bone marrow, kidney, brain etc [23]. It was found that this ACE2 expression is positively correlated with the state of differentiation of the epithelial cells, where well differentiated cells with more ACE2 being the most infected [24]. It is also noted that the expression of ACE2 is highly tissue specific where a greater amount is expressed in cardiovascular, renal and the gastrointestinal systems and less in lung cells showing a considerable impact on cardiac involvement of the disease. Moreover, hypoxaemia can be caused as a consequence of pneumonia due to impaired gas exchange at the alveolar-capillary inter-surface. Further, it may cause apoptosis of cardiac cells [22].

Furthermore, it can cause injuries to other organs including, intestinal mucosa, kidneys and brain [25]. Due to boosted immune and inflammatory responses which occur as a consequence of the viral entry, cytokines can be released in large amounts, leading to multi-organ failure including severe respiratory dysfunction [26].

IV. VIRULENCE

SARS-CoV-2 is a highly contagious virus because of its exponential spread all over the world during a short time span. A reproductive number (R_0) which is the average number of people that could be affected from an already infected person over the infectious period has been calculated by using mathematical models [27, 28]. As long as R_0 is greater than 1, the continuous development of the transmission can occur, thus emphasizing the importance of keeping the R_0 below 1 by means of preventive and control measures [27]. R_0 calculated for SARS-CoV-2 ranged from 2.2 to 2.6 with 6.4 days of epidemic doubling time [27, 28]. Comparatively, R_0 was <1 for the MERS-CoV and therefore, SARS-CoV-2 can be considered as being more virulent than MERS-CoV. R_0 was estimated around 3 for SARS-CoV which indicates high virulence [29].

The incubation period for SARS-CoV-2 is estimated as 1-14 days by WHO and ECDC [30, 31]. This can vary up to 24 days in a minority of people [32]. Since persons below 15 years would have mild symptoms or no symptoms at all, they could act as asymptomatic carriers [27]. SARS-CoV-2 virus is known to be more stable on plastic and stainless steel surfaces for 72 hours and for about 3-4 hours in air indicating the possibility of

disease transmission with the absence of an infected person for hours around [33]. Contrastingly, the sustainability of the viable virus on copper and cardboard surfaces is much lower (4 and 24 hours respectively) compared to plastic and stainless steel. The viable virus was detected on treated wood and cloth for not more than 24 hours. Surprisingly, a noticeable amount of virus was found on the outer layer of a surgical mask for 7 days [34].

V. DETECTION

According to the Center for disease control and prevention (CDC) in USA, the patients who are suspected as being infected with COVID-19 should be initially assessed for clinical symptoms. According to their recommendation, the specimens can be collected for testing from upper respiratory tract (nasopharyngeal swab). If it's unavailable, the lower respiratory tract specimens are also recommended. From patients who are intubated, specimens could be collected by lower respiratory tract aspiration or bronchoalveolar lavage [35]. The most reliable and valid detection method of SARS-CoV-2 is the reverse-transcription polymerase chain reaction (RT-PCR) method [36].

At the very beginning, China was able to detect this novel coronavirus using next generation sequencing of the bronchoalveolar lavage samples that were obtained from the infected patients [37]. This genome sequence was submitted to the NCBI library and was very essential in early identification of the patients with the infection [38]. RT-PCR method based SARS-CoV-2 detection was used at the initial phase of the outbreak, and later on, it was recommended by WHO as a part of recommended protocol for COVID-19 diagnosis [38]. Currently it's being used worldwide for the detection process and plays a very crucial role.

In addition, Loop Mediated Isothermal Amplification (LAMP) is also used for the detection of viral RNA [39]. Moreover, Colloidal Gold Immunochromatography/Lateral Flow Assay are being used most often for the detection of antibody and less commonly for antigen [40, 41]. Moreover, other serological tests using ELISA kits for the identification of IgM and IgG antibodies against SARS-CoV-2 [13] and for detecting viral spike or nucleocapsid proteins [42] are also currently available.

Furthermore, Chest X-rays and computed tomography (CT) scans are also used for the diagnosis of the disease. Chest CT scan images have shown bilateral lung involvements with ground-glass opacities with air bronchograms, increased crazy-wave patterns, ill-defined lung margins, interlobular septal and pleural thickening, cavitations and cystic changes in the infected patients' lungs [43-46].

VI. TREATMENT, PREVENTION AND CONTROL

No vaccine or anti-viral drugs have yet been discovered for the treatment of animal and human corona viruses [47- 49]. Due to their comprehensive sequence diversity, the requirement of safe, stable and readily adaptable vaccines against new corona viruses is emphasized. As a consequence of this, several vaccine types have been developed including, inactivated virus vaccines, live-attenuated virus vaccines, viral vector vaccines, subunit vaccines, DNA or protein vaccines [50]. In addition to vaccines, the efficacy of immune-therapeutics and various drugs have been evaluated in previous viral infections [51, 52]. Drugs that could be potentially effective for the treatment of COVID-19 include remdesivir, lopinavir / ritonavir, lopinavir / ritonavir combined with interferon-β, convalescent plasma, and monoclonal antibodies.

Supportive care includes oxygen therapy, fluid therapy and antibiotics to prevent secondary infections [53]. In addition to the advantages of antiviral treatment, the adverse effects also should be taken into account. For an example, though the early administration of type I interferons are known to be beneficial, the administration in later stages were shown to worsen the symptoms by exacerbating inflammation [13]. Moreover, zinc, chloroquine/ hydroxychloroquine, and Azithromycin are also used as medications though they have not yet been approved by Food and Drug Administration (FDA) for the treatment of COVID-19. A study done by Wang et al., (2020) has shown that most of the patients who were admitted to the ICU were known to be associated with underlying co-morbidities or complications such as old age or diabetes. In this study, they have shown only a fewer number of patients requiring invasive ventilation where most of the patients had required oxygen therapy [20].

Nosocomial transmission was found to have a major impact during both SARS and MERS corona virus outbreaks and in the current COVID-19 [20]. In order to prevent hospital acquired transmission of the infection, all health care workers and the patients who are visiting the clinics should be informed about the special precautions. Specially, the intensivists should follow exact air-bone and droplet precautions while performing aerosol generating procedures [54], the use of personal protective equipment including disposable fluid repellent surgical gowns, gloves, eye protectors, respirators, disinfection procedures in the ICU premises because of the sustainability of the viable virus on various surfaces [55].

VII. CONTROL OF THE INFECTION FROM A SRI LANKAN PERSPECTIVE

Sri Lanka's low infection and death rate per million of people (Table-1) maintained through the country's efforts to counteract the pandemic must be considered satisfactory. It has, indeed, been commended by those at the highest levels of the World Health Organisation, and the European Community Covid-19 monitoring agency. The Institute of Certified Management Accountants (Australia) commissioned a research study to evaluate the Global Response to Infectious Diseases (GRID^{TM}) index to indicate how efficient and effective a country and the preparedness of its health system were in tackling this pandemic and Sri Lanka ranked 10th on the GRID^{TM} Index alongside countries such as Hong Kong and Taiwan [56].

The Ministry of Health and Indigenous Medicine in collaboration with the WHO Country Office for Sri Lanka, has taken initial steps to combat this pandemic by strengthening the control and preventive measures [57]. On 26th of January, 2020, a National Action Committee was appointed in order to prevent the spread of the disease inside the country. The first Sri Lankan local national was confirmed as positive on 10th of March, 2020, a tour guide who was working with Italian tourists.

As of 23rd of March, more than 40 quarantine centers have been established by the Sri Lankan Army to combat the pandemic [58]. As measures to prevent spreading infection, repatriated students and workers were quarantined for two weeks at quarantine centers and the government suspended on arrival visa for tourists. Early travel bans and closure of entry points to the country protected the country from influx of patients. For example, disembarking from several countries was banned on 13th of March, while the Jaffna and Bandaranayake International Airports were closed on the 15th and 17th of March 2020 respectively.

A period of "work from home" was announced by the government for both the public and private sectors. An adequate amount of food and other essential items were dispatched to stores and traders carried out door to door sales during curfew times. General public was asked to stay at home, practice appropriate hygiene methods and self-quarantine methods and to strictly maintain social distancing of 1metre at public places and in the work place. In order to maintain social distancing in public transport, the buses were allowed to carry only half of the passengers could be boarded into disinfected buses and trains of their full capacity.

Also, Sri Lankan Ayurveda Medicine has introduced various indigenous herbs that could be used to boost the immune system in immune-incompetent patients as well as in the general population. As of 30th April 2020, 610 confirmed cases and seven deaths have been reported in Sri Lanka [59]. Many young adults across the country are contributing towards this critical issue by manufacturing health and medical equipment locally that are otherwise very expensive.

Several stark contrasts were noted in some of the strategies that Sri Lanka practiced in handling the pandemic which we believe eventually led to a low infection rate and a death rate. All types of social gatherings including picnics, pilgrimages were banned early in the pandemic. Screening asymptomatic first and second contacts of patients led to early detection of contacts which facilitated isolating them early. The government made use of police, the military and state intelligence service for contact tracing and directing those with suspected exposures for quarantining. All patients with suspected Covid infection were quarantined in regional quarantine centres which were under control of armed forces. Quarantining at government controlled centres seemed to be more effective than quarantining at one's own home. This pre-emptive quarantine facilitated early detection of patients. This led to finding more positives from quarantined persons than from community screening. Everybody who became Covid positive were admitted to the national hospital for infectious diseases. This paved the way to minimize morbidity and mortality due to illness and at the same time helped to prevent further spread of infection. Most of the developed countries admit patients to hospitals only when the patient is seriously ill, especially when there is respiratory distress. With that method apart from the patient being a source for spread of infection, there has been delays in attending to acute illnesses. Once a patient becomes positive for the infection, 'locking down' areas with total severing of contact with outside, imposing curfew in the whole district and banning inter-district travelling helped to localize the outbreak to a geographical pocket. Although it is a tough measure to keep the whole country locked down, it obviously has retarded the upsurge of new cases and helped to flatten the peak of infection.

VIII. CONCLUSION

COVID-19, a severe outbreak which was first experienced by Chinese people in Wuhan city is now continuing to spread over 200 countries, resulting in death of millions of people, morbidities in majority of the affected patients and a severe shrinkage in the global economy. Despite the low fatality rate of SARS-CoV-2 with compared to that of SARS-CoV and MERS-CoV, its high transmissibility and relatively high virulence have led to a significant disease progression, thus making the prevention and control of the disease extremely difficult across the world. COVID-19 is known to severely affect the lower respiratory tract, however causes mild symptoms in the upper respiratory tract. Early detection with the aid of molecular biology tools (RT-PCR, LAMP) together with serological tests (antibody and antigen based immunoassays) and other clinical tests (Chest X-rays and computed tomography (CT) scans) have largely increased the curability of the disease despite the high number of deaths all over the world.

Sri Lanka took a number of drastic control and preventive measures such as pre-emptive quarantining of suspected to be exposed, pre-emptive screening of first and second contacts of patients, social distancing, locking downs areas, imposing curfew and early closing down of entry ports to the country. However, scientists across the world are now facing a daunting challenge in the development of novel vaccines, diagnostic methods, therapeutics and validating the efficacy of already available anti-viral drugs. In this context, a comprehensive understanding of the viral genome sequence, molecular basis of viral entry, replication and infection within the host cell will pave the way for uncovering novel therapeutic approaches and diagnostic ways for the treatment of COVID-19 and to overcome this pandemic as soon as possible.

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