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A Review on Corona Virus Disease 2019 (COVID-19) : Current Status and Future Perspectives

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ABSTRACT

A novel virus, servere acute respiratory syndrome coronavirus-2 (SARS-CoV-2), causing severe acute respiraratory syndrome expanded globally from Wuhan City, Hubei Province, China at the end of 2019. At the beginning of 2020 this virus expands in about 114 countries of the world, and World Health Organization (WHO) declared the SARS-CoV-2 virus a global pandemic in 11th March 2020. In this descriptive review we describe the existing literature with regard to Corona Virus Disease 2019 (COVID-19) epidemiology, pathophysiology, diagnosis, management and future perspective. This review represents a picture of the current status, especially on public health impact, pathophysiology and clinical manifestation, diagnosis, preparedness and emergency response.

Key words : COVID-19, pandemic : preparedness : pathogenesis.

INTRODUCTION :

A series of pneumonia cases of unknown cause emerged in November 2019 in Wuhan City, Hubei Province, China. After few weeks in January 2020 deep sequencing analysis from lower respiratory tract samples identified a novel virus Severe Actue Respiratory Syndrome Corona Virus-2 (SARS-CoV.-2) as causative agent. On 11th February 2020. World Health Organization (WHO) named the disease caused by the SARS-CoV-2 as Covid-19 (Corona Virus Disease-2019). After one

month on 11th March 2020 when the 114 countries are affected with more than 118000 cases and over 4000 death, the WHO declared the Pandemic status.

The virus of COVID-19 is single stranded RNA virus, with a typical crown like appearance seen under an electron microscope due to the presence of glycoprotein spikes on its envelope. It is not the first time that a Corona Virus causing an epidemic has been a significant global health threat in November 2019, on outbreak of Corona Viruses (Co.Vs) with severe acute respiratory syndrome corona virus (SARS-Co.V) started in the year 2002 in Guangdong Province, PR China and again in September 2012 the middle east respiratory syndrome corona virus (MERS-Co.V) appeared in Saudi Arabia. There are four genera of corona viruses are reported - (i) Alpha-Corona Virus (α-Co.V); (ii) Beta Corona Virus (β- Co.V); (iii) Delta Corona Virus (δ- Co.V); and (iv) Gamma Corona Virus (γ-Co.V). The virus has a natural and zoonotic origin; two scenanarios that can plausible explain the origin of SARS-Co.V-2 are - (i) Natural selection in an animal host before zoonotic transfer. (ii) Natural selection in humans following zoonotic transfer. Clinical features and risk factors are highly variable, making the clinical severity range from asymptomatic to fatal. This review aims to summarize early findings on the epidemiology, clinical features, diagnosis, management and prevention of COVID-19.

EPIDEMIOLOGY:

The COVID-19 epidemic in early December from Wuhan City, Hubei Province, China and was then exported to a number of countries. The first confirmed case of COVID-19 outside China was diagnosed on 13th January. 2020 in Bangkok (Thailand). On 2nd march 2020. 67 territories outside mainland China has reported 8565 confirmed cases of COVID-19 with 132 deaths, as well as significant community transmission occurring in several countries world wide, including Iran and Italy and it was declared a global pandemic by WHO on 11th march 2020.

Today, 8th June 2020, based on WHO reports, we have globally 70,00000 confirmed cased and 400000 deaths, The top 10 most affected countries are - **United State** 1900000 $\pm$ 23408 confirmed cases and 112000 $\pm$ 723 deaths; **Brazil** 692000 $\pm$ 27075 confirmed cases and 36499 $\pm$ 904 death; **Russia** 470000 $\pm$ 8000 confirmed cases and 5859 $\pm$ 134 deaths; **United Kingdom** 286000 $\pm$ 1326 confirmed cases and 40542 $\pm$ 0 deaths; **India** 247000 $\pm$ 1000 confirmed cases and 6929 $\pm$ 287 deaths; **Spain** 242000 confirmed cases and 27136 death; **Italy** 235000 $\pm$ 197 confirmed

cases and 33899 ± 53 deaths; **Peru** 197000 ± 4360 confirmed cases and 5465 ± 139 deaths ; **Germany** 186000 ± 301 confirmed cases and 8776 ± 22 deaths; **Iran** 172000 ± 2364 confirmed cases and 8281 ± 72 deaths;

The five low affected territories from COVID-19 are - **Vatican city** 12 confirmed cases and all recovered; **Greenland** 13 confirmed cases and all recovered; **Falkland Island** 13 confirmed cases and all recovered; **Fiji** 18 confirmed cases and all recovered; **Dominica** 18 confirmed cases with 16 recovered; and 2 deaths.

PATHOPHYSIOLOGY AND CLINICAL MANIFESTATIONS:

To address the pathogenic mechanisms of SARS-Co.V-2 its viral structure and genome must be considered. Corona Viruses are enveloped positive sense RNA viruses, with the largest known RNA genomes of ~ 30 kb. The genome contains a 5` cap structure along with a 3` poly (A) tail, allowing it to act as an mRNA for translation of the replicase polyproteins. Starting from the viral RNA, the synthesis of polyprotein 1a/1ab (pp 1a/pp 1ab) in the host is realized. The transcription works through the replicon-transcription complex (RTC) organised in double member vesicles and via the synthesis of subgenomic RNAs (ss RNAs) sequences. Transcription termination occurs at transcription regulatory sequences, located between the so called open reading frames (ORFs), that work as templates for the production of sub genomic mRNAs.

The pathogenic mechanism that produces pneumonia seems to be particularly complex. The data so for available seen to indicate that the viral infection is capable of producing an excessive immune reaction in the host. In some cases, a reaction takes place, which as a whole is labelled a cytokine storm". The effect is extensive tissue damage. The protagonist of this storm is interleukin-6 (IL-6). IL-6 is produced by activated leucocytes and acts on a large number of cell and tissues. IL-6 increases during inflammatory disease, infections, autoimmune disorders, cardiovascular disease and some types of cancer. It is also implicated in the pathogenesis of the cytokine release syndrome (CRS) that is an acute systemic inflammatory syndrome by fever and multiple organ disfunction.

The virus might pass through the mucous membranes, especially nasal and larynx mucosa, then enters the lungs through respiratory tract. Then the virus would attack the targeting organs that express angiotensin converting enzyme-2 (ACE-2), such as the lungs, heart, renal system and

gastrointestinal tract. The virus begins a second attack, causing the patient's condition to aggravate around 7 to 14 days after onset. B-lymphocyte reduction may occur early in the disease, which may affect antibody production in the patient.

Asymptomatic infections have also been deseribed, but their frequency is unknown. The main symptoms are Fever, Cough, Dyspnea, Headach, Sore throat, Rhinorrhea etc. Pneumonia appears to be the most frequent serious manifestation of infections characterized primarily by fever, cough, dyspnea and bilateral infiltrates on chest imaging. There are no specific clinical features that can yet reliably distinguish COVID-19 from other viral respiratory infection. Respiratory droplet transmission in the main route and it can also be transmitted through person to person contact by a asymptomatic carriers.

Chest CT in patient with COVID-19 most commonly demonstrates ground-glass-opacification with or without consolidative abnormalities, consistent with viral pneumonia. Chest CT abnormalities are more likely to be bilateral, have a peripheral distribution, and involve the lower lobes. Less common findings inside pleural thickening, pleural effusion and lymphadenopathy. Chest CT may be helpful in making the diagnosis but no finding can completely rule in or rule out the possibility of COVID-19. The possibility of COVID-19 should be considered primarily in patients with onset fever and/or respiratory tract symptoms such a cough and dyspnea. It should also be considered in patients with severe lower respiratory illness without any clear cause.

The period from the onest of COVID-19 symptoms to death ranges from 6 to 41 days with a median of 14 days. This period is dependent on the age of the patient and status of the patient's immune system. It was shorter among patients >70 years old compared with those under the age of 70 years.

The WHO has reported an incubation period for COVID-19 between 2 to 10 days. However some literature suggests that the incubation period can last longer than two weeks and it is possible that a very long incubation period could reflect double exposure. Many studies support a 14 day medical observation period for people exposed to the pathogen. The severity of the clinical picture seems to be correlated with age (>70 years), comorbidities such as diabetes, chronic obstructive pulmonary disease (COPD), hypertension, obesity and male sex but currently no scientifically valid explanation have been developed.

DIAGNOSIS:

The patient with suspected infection, the following diagnosis techniques are utilised; (i) Rapid and accurate detection of SARS-Co.V-2 is essential to control the outbreak of COVID-19, (ii) Revers transcription quantitative PCR (RT-qPCR) is a molecular biological diagnosis technology used to detect the positive nucleic acid of SARS Co.V-2 in sputum, throat swabs and secretion of the lower respiratory tract samples. In patient with COVID-19, the white blood cell count can vary, leukopenia, leukocytosis and lymphopenia have been reported, although lymphopenia appears most common. Elevated lactate dehydrogenase and ferritin levels are common and elevated aminotransferase levels have also been described. On admission many patients with pneumonia have normal serum procalcitonin levels, however, in those requiring ICU care, they are more likely to be elevated. High D-dimer level and more severe lymphopenia have been assoicated with mortality. Image finding - Chest CT in patient with COVID-19 most commonly demonstrates ground-glass opacification with or without consolidative abnormalities, consistent with viral pneumonia.

An oropharyngeal swab can be collected but is not essential : if collected, it should be placed in the same container as the nasopharyngeal specimen. An oropharyngeal swab is an acceptable alternative if nasopharyngoal swab is unavailable. Expectorated sputum should be collected from patient with productive cough; induction of sputum is not recommended. Data from this study suggested that viral RNA levels are higher and more frequently detected in nasal swab as compared with oral swab.

A positive test for SARS-Co.V-2 generally confirm the diagnosis of COVID-19, although false-positive test are possible. If initial testing is negative but the suspicion for COVID-19 remains, WHO recommends resampling and testing from multiple respiratory tract sites. The accuracy and predictive values of SARS-Co.V-2 testing have not been systematically evaluated, Negative RT-qPCR tests on oropharyngeal swabs despite CT findings suggestive of viral pneumonia have been reported in some patients who ultimately tested positive for SARS-Co.V-2. Serologic test, once generally available should be able to identify patients who have either current or previous infection but a negative PCR test.

MANAGEMENT OF DISEASE:

There is no antiviral treatment recommended for COVID-19, and no vaccine is currently available. The treatment is symptomatic and oxygen therapy represents the major treatment intervention for patients with severs infection. Mechanical ventilation may be necessary in cases of respiratory failure refractory to oxygen therapy; where as hemodynamic support is essential for managing septic shock. Different strategies can be used depending on the severity of the patient and local epidemiology. Home management is appropriate for asymptomatic patients. They need a daily assessment of body temperature, blood pressure, oxygen saturation and respiratory symptoms for about 14 days. The prevention of transmission to others in most important during management of such patient. and provides prompt hospitalization when required. Outpatients with COVID-19 should stay at home and try to separate themselves from other people of the family. The optimal duration of home isolation is uncertain. but in consideration of incubation time around 14 days without symptoms are considered sufficient to end home isolation. Patient with severs disease often need oxygenation support. High-flow oxygen and noninvasive positive pressure ventilation have been used.

The main pharmacological options for Corona Virus Disease 2019 (COVID-19) are summarised as follows -

1. Glucocorticoids

2. Remedesivir

3. Chloroquine and hydroxychloroquine

4. Tocilizumap

5. Lopinavir - ritonavir

6. Baraticinib

7. Non-steroidal anti inflammatory drugs

8. Angiotensim converting enzyme-2

Glucocorticoids should not be used in patients with COVID-19 pneumonia unless there are other indications e.g., exacerbation of chronic obstructive pulmonary disease. Glucocortiocoids have been associated with an increased risk for mortalily in patients with influenza and delayed viral clearance in patients with MERS-Co.V infection.

Remedesivir is a noval nucleotide analogue that has activity against SARS-Co.V-2 in vitro and related corona virus (SARS-Co.V and MERS-Co.V) both in vitro and animal studies. Any clinical impact of rememdesivir on COVID-19 remains unknown.

Chloroquine and hydroxycholoroquine have antiviral activity in vitro, as well as anti-inflammatory activities. They act on interference with the cellular resceptor ACE-2, on impairment of acidification of endosomes and on activity against many pro-inflammatory cytokines (eg. IL-1 and IL-6).

Tocilizumab is a recombinant humanized monoclonal antibody which is binds to the interleukin-6 (IL-6) receptor and blocks it from functionating. It is used for patient with severe COVID-19 and elevated IL-6 levels; the agent is being evaluated in a clinical trial.

Lopinavir-ritonavir appears to have little to no role in the treatment of SARS-Co.V-2 infection. This combined protease inhibitor, which has primarily been used for HIV infection and has invitro activity against the SARS. Co.V.and appears to have some activity against MERS-Co.V in animal studies.

Support oxygen therapy with high flow nasal oxygen should be used only in selected patients with hypoxemic respiratory failure. Compare with standard oxygen therapy, High-flow nasal oxygen reduces the need for incubation.

TRADITIONAL THERAPY:

Traditional medicine system, Ayurveda is amongst one of them and now, the top group of scientists from Indian Institute of Technology (IIT) Delhi, in most potent and widely used Ayurvedic herbs "Ashwagandha' may hold strong potential in fighting COVID-19. A combined study from IIT Delhi's DAILAB and Japan's National Institute of Advanced Industrial Science and Technology (AIST) made the discovery that Ashwagandha can prove to be the crucial medicine in fighting corona virus and can be even used in the development of a vaccine.

Just recently, India's Ministry of AYUSH and CSIR announced a slew of measures and clinical trials aimed at studying the use of Ashwagandha, along with other Ayurvedic herbs as a preventive treatment to front line workers and infected patients in a large study which is to start

soon. Other medicine under study include Ashwagandha, Guduchi, Yasthimadhu, Peepli, Tulsi Ginger and another formulated drug. 'Ayush 64' which will be tested close to 50000 people.

The study, which is soon to be published found that 'Ashwagandha' in particular, contains some natural biochemical compounds which can work the same way as other anti-corona virus drugs. The use of Ayuvedic medicines in some cases is also being studied for its prophylectic used and hence, has been termed as an anti-virual remedy.

PREVENTION:

Prevention is, so far, the best practice in order to reduce the impact of COVID-19 considering the lack of effective treatment. At the moment, there in no vaccine available and the best prevention is to avoid exposure to the virus. The main preventive measures for Corona Virus Disease 2019 (COVID-19) are as follows :

1.   To use face masks or respirator (N 95), when moves outside home.

2.   To cover coughs and sneezes with tissue papers.

3.   To wash hands regualarly with soap or hand sanitizer containing at least 60% alcohol.

4.   To avoid contact with infected people.

5.   To maintain an appropriate distance (2 meter or 6 feet) from people.

6.   To refrain from touching eyes, nose and mouth with unwashed hands.

7.   Helth workers always use PPE kit when in contact with infected person.

8.   To use "Ayurvedic Kadha" (preventive home remedy) daily which protect us our body against viral infections.

9.   In case of symptoms (eg. fever, cough and difficulty breathing seek medical care early.

10.   Stay informed and follow advise given by your health care provider.

FUTURE PERSPECTIVES:

The COVID-19 outbreak is proving to be an unprecedented disaster, especially in the most afficited countries China, Italy Iran USA and India in all aspects, especially health, social and economic. It is too early to forecast any realistic scenario, but it will have a strong impact world wide. If high income countries, especially those already effected by the outbreak, seem to face a catastrophic perspective, in low-income countries there seem to be two possible scenarios. In particular, in the worst-case scenario, when the COVID-19 outbreaks, the majority of countries will be unprepared, with low resources allocated for affording the viral emergency and the consequences will be catastrophic. If the preventive measure will be implemented, we could register a low incidence of hygine linked diseases that still represent leading causes of death.

CONCLUSION:

This review, provides and insight in the the COVID-19 current situation and represent a picture of the current state of public health impact, pathophysiology and clinical manifestations, diagnosis, case management, emergency response and preparedness. This review provides good knowledge about prevention, management of COVID-19, Ayurvedic medicines and traditional therapy, thus we hopeful that it will help in finding the best practice for the management and treatment of symptomatic cases. Only once this pandemic ends, one will be able to assess the health, social and economic impacts of this global disaster.

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