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OVERVIEW ON CORONAVIRUS DISEASE 2019(COVID-19): IT'S PROGNOSTIC FACTORS; PSYCHOSOCIAL IMPACT AND CURRENT TREATMENT

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ABSTRACT

COVID-19 pandemic is threatening all over the world with the emergence and it's rapid spread. This virus begun as an outbreak in Wuhan, china in December 2019. As of 13th July 2020, there have been 13 million confirmed cases of COVID-19 globally with 5.7 lakhs deaths. Symptoms include mild to severe which worsens the patient condition that may leads to death. Some prognostic factors like diabetes, hypertension, age, sex, weather conditions and smoking are influencing the rapid rate of spread and progression of COVID-19. Diagnosis is done through molecular tests on respiratory samples. Currently there is no vaccine and approved medication, only investigational treatments are suggested like azithromycine, hydroxychloroquine, remdesivir, ribavarin, interferon, corticosteroids, umifevir, inhibitor vitamin-C and vitamin-D. World health organisation (WHO) declares that the preventive and supportive measures are the only strategy to reduce and control this pandemic. The WHO has issued specific psychosocial considerations for abating the growing stigma of COVID-19.

KEYWORDS: COVID-19, Prognostic factors, Psychosocial, Azithromycine.

1. INTRODUCTION

World is facing a mysterious pneumonia which is characterized by fever, dry cough, fatigue and occasional gastrointestinal symptoms happened in sea food wholesale market, in Wuhan, Hubei China in December 2019.[1] Spread and transmission of this disease is occurring through airborne transmission of aerosols produced by asymptomatic individuals during breathing and speaking.[2,3] Officially the World Health Organization (WHO) announced name of the 2019 coronavirus as coronavirus disease (COVID-19) or Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-Cov-2).[4] Since December 2019, it is spreading to become world pandemic with alarming morbidity and mortality.

Accordingly, SARS-Cov-2 infection can be roughly divided into three stages, Stage 1: an asymptomatic incubation period with or without detectable virus, Stage 2: non-severe symptomatic period with the presence of virus, Stage 3: severe respiratory symptomatic stage with high viral load.[5] The symptoms of COVID-19 infection appear after an incubation period of approximately 5.2 days. The period from the onset of symptoms to death ranged from 6-41 days with the median of 14 days.[6] This period depends on age & status of patient's immune system. Fever was the most frequent symptom and cough is the second most common symptom observed,[7] the other symptoms includes the characteristics of influenza like disease i.e sore throat, headache, myalgia, asthenia, diarrhea and eventually dyspnea.[8] It also includes symptoms such as olfactory or taste dysfunction which were evidenced along with the development of the pandemic.[8,9]

SARS-Cov-2 is a beta-coronavirus belonging to the family *coronaviridae*.[10] In 2003, a new coronavirus originated from Southeast China, especially Guangdong province and was named as SARS coronavirus that fulfilled the Koch's postulate.[1] Due to lack of proper treatment and vaccine for SARS, the emergence of another outbreak in 2012 of novel coronavirus in Middle East Respiratory Syndrome (MERS) shared similar features with the outbreak in 2003.[1] In the aftermath of the SARS and MERS epidemics, intense efforts were developed to identify the animal reservoirs of these viruses and to reconstruct the chain of events that led to the human spillovers. It is now known that both viruses originated in bats and were transmitted to humans by intermediate hosts.[11]

The origin of the SARS-Cov-2 genome has been linked to bats akin to SARS-Cov-1 and MERS-Cov viruses.[12] This viruses undertake residence in the intermediate hosts shown in **Table 1,** it was suspected that in SARS-Cov-2 pangolins were the natural reservoir.[12]

Furthermore cases associated with travel has been identified for SARS, MERS and COVID-19. Due to global transportation & negligence of people in maintaining and following preventive measures, there is increase in spread of disease throughout the world.

Table 1: Summary of the natural reservoir, intermediate host and target in major coronavirus.

Virus (Disease)	Origin virus	Intermediate host	Host
SARS-CoV-1 (SARS 2002)	SARS-like bat-CoV	Civet cat	Humans
MERS-CoV (MERS 2012)	SARS-like bat-CoV	Camel	Humans
SARS-CoV-2 (COVID 2019)	BaT-CoV RatG13	Pangolin	Humans

Given spread of the new coronavirus and its impacts on human health, the research community has responded rapidly to the new virus and many preliminary research articles have already been published about this epidemic. We conducted a scoping review to summarize and critically analyze all the published scientific articles regarding the new coronavirus. This review aims to provide the evidence of early findings on the origin, epidemiology, pathogenesis, psychosocial impact, prognostic factors, clinical diagnosis as well as prevention and control of COVID-19. This review can provide meaningful information for future research related to this topic and may support government decision making on strategies to handle this public health emergency at the community, national and international levels.

2. Epidemiology

Illness of the COVID-19 is spreading rapidly and globally, till 13th July, 2020 13 million people were affected by the disease throughout the world. The first laboratory case was confirmed on December 1, 2019 in Wuhan, china. As of January 1, 2020, a total of 59 suspected cases with fever and dry cough were referred to a designated hospital,[1] of the suspected cases 41 patients were confirmed by next generation sequencing through reverse transcription polymerase chain reaction (RT-PCR). The first exported case was in Thailand on January 13, 2020.[1] As of January 22, 2020 a total of 571 cases of the COVID-19 were reported in China.[6] Till January 30, 2020 7734 cases have been confirmed in china and the other 90 cases have been reported from different countries.[6] As of February 6, 2020 a total of 28276 confirmed cases with 565 deaths were documented by WHO, involving minimum of 25 countries.[1] As of March 21, 2020 there have been 3,04,900 cases with 13001 deaths of which 94,793 have been recovered.[12]

A more useful and unbiased indicator to assess the disease severity is mortality rate in relation to the population size. The Nations with greater proportion of elderly individuals are at high risk to pandemic. It is the main factor responsible for a lower disease burden and mortality in South Asian countries.[13]

On 13th July, 2020 the total no. of COVID-19 cases throughout the world were found to be 13 million and total no. of active cases were found to be 4 million with total no. of deaths were 5,72,212. The death rate and the recovery rate were reported as 4.38% and 58.25% (7.6 million). In India as of July 13th, 2020 total no. of COVID-19 cases were found to be 8,79,902 and total active cases were 3,01,795 and with total no. of deaths 23,200. The total no. of patients recovered were 5,54,907. Day by day the total no. of cases were increasing due to lack of definate treatment and vaccine.

It is clear that COVID-19 infection occurs through exposure to virus, both the immunosuppressed and normal population were appear to be susceptible. Some studies have reported an age distribution of adult patients between 25 and 89 years old. Most adult patients were between 35 and 55 years old and they also identified cases among children and infants. A study on early transmission dynamics of the virus reported the median age of patients to be 59 years, ranging from 15 to 89 years, with the majority(59%) being male.[4] It was suggested that the population most at risk may be people with poor immune function such as older people and those with renal and hepatic dysfunction.[1]

3. Mode of Transmission: The latest guidelines from health authorities described three main transmission routes from COVID-19.

- Droplet transmission
- Contact transmission
- Aerosal transmission

3.1 Droplet transmission: Droplet transmission occurs when respiratory droplets are ingested or inhaled by individuals nearby in close proximity. [4] Respiratory infections are due to the transmission of virus containing droplets (> 5-10 μm) and exhaled from infected individual during breathing, speaking, coughing, and sneezing.[2]

3.2 Contact transmission: Contact transmission may occur when a subject touches a surface or object contaminated with virus and subsequently touch their mouth, nose, or eye. [4]Additional considerations must be done regarding the residence time of the SARS-CoV-2 virion on surfaces. The viable residence time of SARS-CoV-1 in aerosols, copper, cardboard, stainless steel, and plastic are 3h, 4 h, 24 h, 48 h, and 72 h, respectively.[12]

3.3 Aerosal transmission: Aerosal transmission may occur when respiratory droplets mix into air, forming

aerosal which may pose a risk of exposure at distance beyond 1-2 m from an infected individual.[3,4] The respiratory particles of generally (< 5 µm) are present in air for prolonged periods.[14] However a large proportion of spread of SARS-COV-2 are occuring through airborne transmission produced by asymptomatic individual during breathing and speaking.[2]

In addition to these routes, some studies also reported that the digestive system as a potential transmission route for COVID-19 infection. Since patient had abdominal discomfort and diarrheal symptoms, researchers analyzed four datasets with single cell transcriptomes of digestive system. They also concluded that ACE 2 was highly expressed in absorptive enterocytes from ileum and colon.[4] The virus is also present in the stool and contamination of water supply and subsequent transmission occurs via aerolized fecal-oral route.[4]

4. Virion and Pathogenesis

SARS-COV-2 is a positive sense, zoonotic in nature, single stranded RNA, enveloped virus that is 50-200nm in diameter. The genomic RNA is 30 kb, one vital encoded structural protein is the spike glycoprotein (S) that consist of three S1, S2 heterodimers that binds to Angiotensin Converting Enzyme (ACE-2) receptor on type -II pneumocyte and the other surface protein is the hemagglutinin-esterase (HE) dimer as shown in Figure 1. The entry of SARS-COV-2 into type-II pneumocyte is via endocytosis and then multiplies in the cytoplasm Additionally, the RNA from the SARS-COV-2 acts as pathogen-associated-molecular- pattern (PAMP) and will be recognised by pattern recognition receptor.[12]

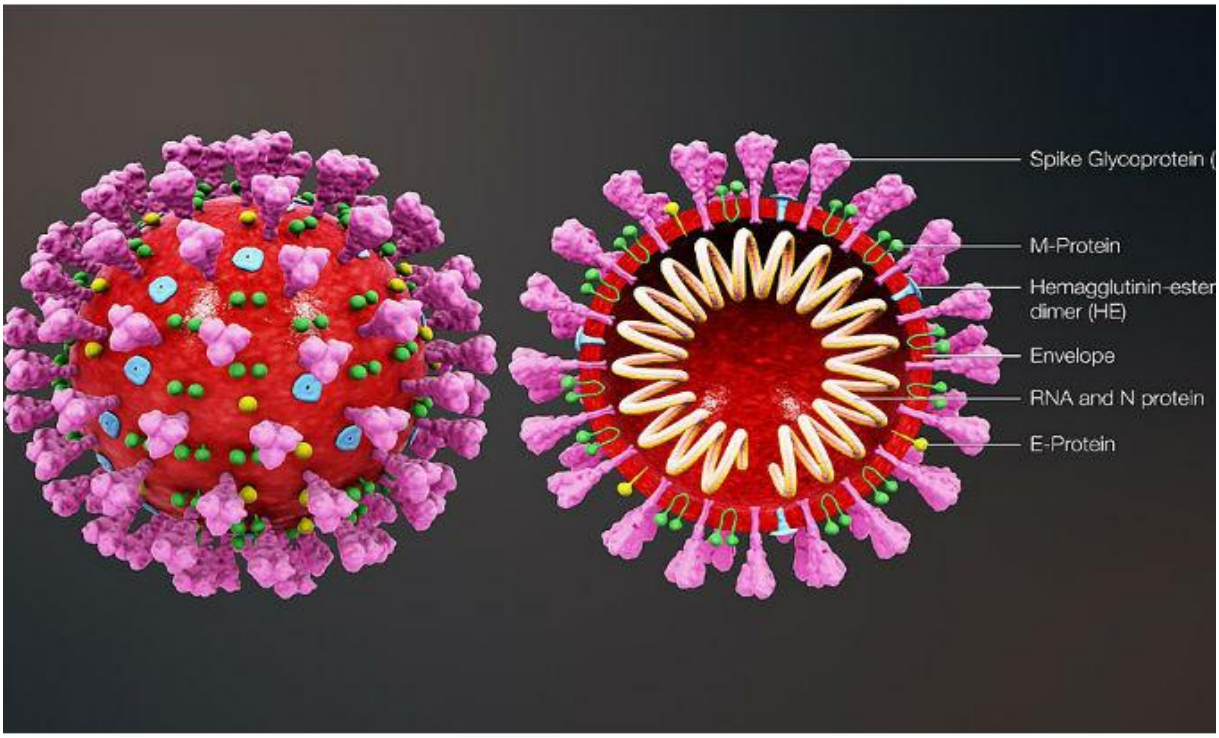

Figure 1: Structural representation of COVID-19.

The main pathogenesis of COVID-19 infection targeting respiratory system leading to severe pneumonia, RNA aemia, combined with the incidence of ground-glass opacities and acute cardiac injury.[6]

4.1 Angiotensin converting enzyme (ACE) 2: ACE2 serves as the receptor for SARS-COV-2 and is also involved in modulating the effect of virus on lung injury. Increase in interferon expression and ethnic variations in host interferon response which could be a key factor in modulating viral replication after infection.[13] Viral infection will cause the imbalance of T- helper-1 and T-helper- 2 responses and induce an inflammatory storm by increasing the level of inflammatory factors such as IL-4, IL-10, IL-6. Inflammatory storm in critical patient release cytokines causing systemic immune injury which may leads to multiple organ failure and even death.[15] An analysis of the polymorphism in 25 European countries found that prevalence as well as severity of COVID-19 correlated with ACE D allele frequency and about 38% of variability could be explained by the relative frequency of ACE 1D – allele.[13]

4.2 Host cell protease: Host cell protease namely transmembrane serine proteases (TMPRSS), furin, trypsin, plasminogen have a crucial role in viral entry by causing the cleavage of 'S' protein and triggering it's binding to ACE2 receptor. Co-expression of ACE 2 and

TMPRSS in type-2 alveolar cells is important for viral entry and it's replication.[13]

4.3 C-ATP: The C-ATP level is potentially considered as crucial component in the infectivity and prognosis of COVID-19. There are several approaches to improve C-ATP. Most of them are easily available through lifestyle changes. First regular exercise improve mitochondrial respiratory capacity through an increase in PGC-1-α. Smoking cessation is second approach to improve mitochondrial capacity and improvement in C-ATP.[16]

Although respiratory system is the main target of COVID19, other systems like renal, neurological, immune and cutaneous have been reportedly affected.[17] Although producing various growth factors, MSC's (mensenchymal stromal cells) may help in repair of damaged lung tissue.[5] Lung damage is a major hurdle to recovery in the severe infected patient.

5. Immunology

Clinically, the immune response induced by SARS-COV-2 infection are two phased. During the incubation and mild stages of SARS-COV-2 infection, a specific adaptive immune response is required to eliminate the virus and to preclude disease progression to severe stages. However, when a protective immune response is impaired, virus will propagate and massive destructive of affected tissue will occur, especially in organs that have high ACE 2 expression, such as intestine and kidney. The damaged cells induce innate inflammation in the lungs that is largely mediated by pro- inflammatory macrophages and granulocytes. Therefore need of strategies to boost immune response (anti-sera, or pegylated IFN alpha) at this stage are certainly important.[5]

5.1 HLA Haplotypes: The major-histocompatibility-complex antigen loci (HLA) are the prototypical candidates for genetic susceptibility to infectious diseases. Haplotype HLA-loci variability results from selective pressure during co-evolution with pathogens. Immunologists have found that T-cell antigen receptors, on CD4+ or CD8+ T cells recognize the conformational structure of the antigen-binding-grove together with the associated antigen peptides. Therefore, different HLA haplotypes are associated with distinct disease susceptibilities. The repertoire of the HLA molecules composing a haplotype determines the survival during evolution. Accordingly, it seems advantageous to have HLA molecules with increase binding specificities to SARS-COV-2 virus peptides on the cell- surface of antigen presenting cells. It is imperative to study whether specific HLA loci are associated with the development of anti-SARS-COV-2 immunity and, if so, to identify the alleles, either class I or II, that demonstrate induction of protective immunity. Once the dominant alleles are identified, simple detection kits can be developed. Such information is critical for (1) strategic clinical management; (2) evaluation of the efficacy of vaccination in different individuals in the general population; (3) assignment of clinical professional and managerial teams amid interactions with COVID-19 patients.[11]

5.2 Hyaluronan: a potential cause of fatalities

The innate immune response to tissue damage caused by the virus could lead to acute respiratory distress syndrome (ARDS), in which respiratory failure is characterized by the rapid onset of widespread inflammation in the lungs and subsequent fatality. The symptoms of ARDS patients include short/rapid breathing, and cyanosis.

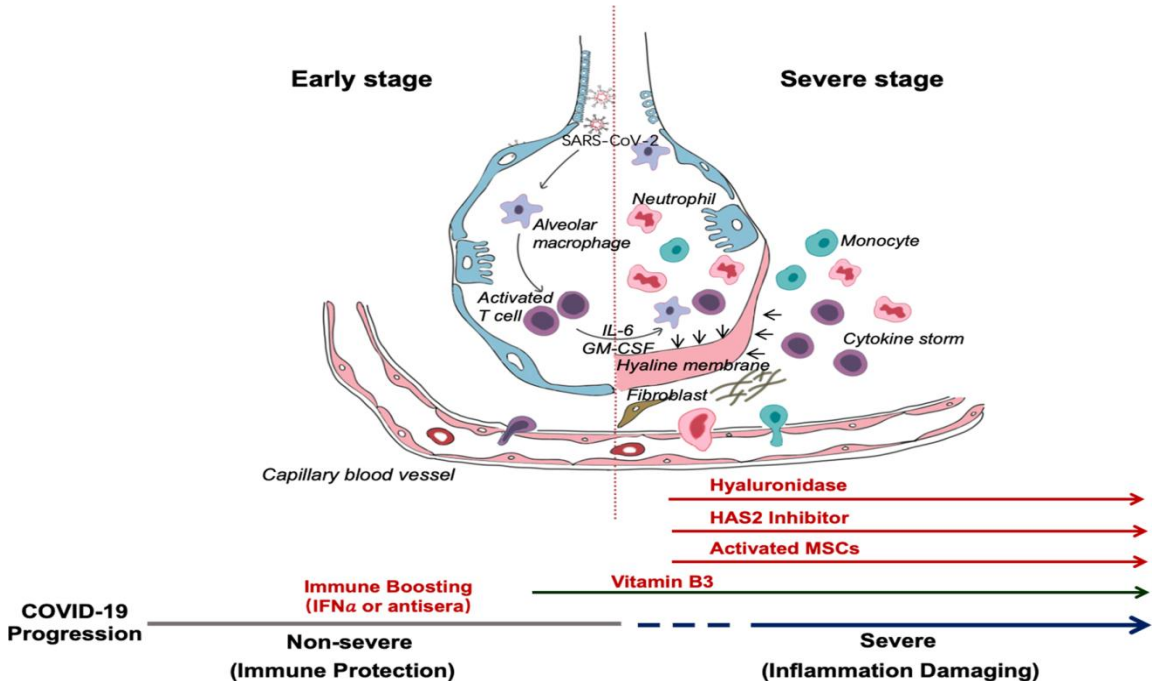

Fig. 2: Diagramatic representation of the progression of COVID-19 infection.

Severe patients admitted to intensive care units often require mechanical ventilators and those unable to breath have to be connected to extracorporeal membrane oxygenation (ECMO) to support life.CT images revealed that there are characteristic white patches called "ground glass", containing fluid in the lungs. Recent autopsies have confirmed that the lungs are filled with clear liquid jelly, much resembling the lungs of wet drowning. Although the nature of the clear jelly has yet to be determined, hyaluronan (HA) is associated with ARDS; moreover, during SARS infection, the production and regulation of hyaluronan is defective. The levels of inflammatory cytokines (IL-1, TNF) are high in the lungs of COVID-19 patients and these cytokines are strong inducers of HA-synthase-2 (HAS2) in CD31+ endothelium, EpCAM+ lung alveolar epithelial cells, and fibroblasts. Importantly, HA has the ability to absorb water up to 1000 times its molecular weight. Therefore, reducing the presence or inhibiting the production of HA holds a great promise in helping COVID-19 patients breathe. Doctors can simply provide patients medical grade hyaluronidase to reduce the accumulation of HA and thus to clear the jelly in the lung. In animal models, influenza induced breathing difficulties can be relieved by intranasal administration of hyaluronidase. Doctors can also use a clinically approved bile therapy drug, Hymecromone (4- Methylumbelliferone, 4-MU), an inhibitor of HAS2.[11]

6. Prognostic Factors

The patient with underlying comorbidities like Diabetes, Hypertension, Cardiovascular diseases, Respiratory diseases, Obesity are having high risk of developing serious events like ICU admissions, mechanical intubation, and even death.

6.1 Diabetes: The high prevalence of diabetes globally makes it a frequent comorbidity in patient with COVID-19. In most studies patient with diabetes who develop COVID-19 have been seen to have a worse prognosis and may increase mortality,[18] Increased viral replication in diabetes may also due to an increase in furin, which is type-1 membrane bound protease involved in entry of coronavirus into the cell.[18] Beta cells infected by SARS-COV-2 may reduce insulin secretion.[19] In this context, it is important to note that there is a strong association between type-2 DM, Obesity and abnormal secretion of adipokines and cytokines like TNF- alpha and interferon which may further impair immunity and predispose to increase severe infection.[18]

6.2 Hypertension is the most common cardiovascular comorbidity which significantly increases the mortality risk in COVID-19.[20]

To the best of our knowledge this could be most updated review:

- Presence of Chronic-Obstructive-Pulmonary-Diseases(COPD) had a 6.6 times higher risk of developing serious events in COVID-19.[21] Early identification and adequate treatment of SARS-COV-2 at high risk for acute respiratory failure are paramount to avoid ARDS and end organ damage.[22]
- Presence of Chronic Kidney Disease (CKD) had a 5.3 fold increased risk having serious events.
- Presence of Cardiovascular diseases (CVD) had 4-5 times greater chances of progressing to severe events.
- The presence of Diabetes had 3.07 fold higher chances of impact on death in SARS-COV-2.[21]

6.3 Age: Age seems to be a significant predictor of death in SARS-COV-2 infected patient admitted to hospital, particular due to presence of comorbidities, such as cardiovascular disease and Chronic-Obstructive-Pulmonary-Diseases (COPD). [11,23] The absence of immunity and lack of definitive medicines leads to high risk of disease spread amongst elderly population.

6.4 Male gender: While men and women have the same susceptibility to SARS-COV-2, men are prone to higher morbidity and mortality independent of age. This difference can be justified by the cell energy hypothesis. Estrogens (sex steroid of females) are potent stabilizers of ATP production during oxidative stress (during SARS-COV-2 induced inflammation) [17]. It was found that women are less susceptible to viral infection, to maintain C-ATP which plays an important role in innate and adaptive immunity.[15,16]

6.5 Weather conditions: The extreme weather conditions might play a role in rapid spread of the virus. Latitude and seasonality may also predict potential spread of COVID-19. Climatic conditions like temperature, rainfall and wind speed might be a biological catalyst for interaction between COVID-19 and human.[7]

6.6 Tobacco smoker: The risk of long lasting and serious COVID-19 infection is more among tobacco smokers. Apart from a direct effect on lung parenchyma and decrease in pulmonary capacity, they can potentially induce immune dysfunction through a decrease in ATP content of immune cells. This can be due to nicotine-induced mitochondrial dysfunction. The resultant ATP-depletion increase the risk of immune dysregulation by COVID19.[16]

7. Psychosocial Impact

This unpredictable, fast spreading infectious disease has been causing universal awareness, anxiety and distress, all of which according to WHO are natural psychological response to the randomly changing conditions. Prior studies reported that mental well-being had been heavily affected in this kind of global pandemic. Therefore it is imperative to determine the various possible ways in which SARS-COV-2 pandemic will be impacting the world's mental health. [24] Patient infected with COVID-19 experienced physical discomfort, fear of developing

complications, and discrimination from mass media. These negative feelings could lead to elevated risk of psychiatric problems, particularly depressive symptoms. Moreover since infected people were treated in isolation hospitals, with loneliness, anger, anxiety, depression, insomina and social isolation which could trigger depression as well.[24,25] The WHO has also issued specific psychological considerations for abating the growing stigma of COVID-19. Health crime originated out of the fear of being corona positive has also been reported from India,[24] Previous outbreak have reported that psychological impact of quarantine may leads to irritability, fear of contacting, and patient spreading infection to family members were likely to suffer from depression due to excessive psychological pressure ,guilt about transmission, and also to extreme of consequences including suicide.[24,25] However they uncertainly develop some Obsessive-Compulsive symptoms like repeated temperature checks and sterilization. Effects such as Post- traumatic stress disorder (PTSD) have been reported, symptoms of which have been positive associated with duration of quarantine.[24] One study highlighted the services that were being provided in china and suggested a list of strategies for general public to minimize outbreak-related stress: 1) assessment of accurate information 2) enhancing social support, 3) reducing the stigma associated with the disease, 4) maintaining a normal life as feasible while adhering to safety measures, 5) use of available psychosocial services, particularly online services when needed. Above mentioned strategies would empower society to handle the COVID-19 outbreak in an adaptive manner.[26] Apart of these, another important aspect is stigmatization and societal rejection regarding the quarantined cordon in forms of discrimination, suspicion and avoidance by neighbour-hood, insecurity, workplace prejudice, withdrawal from social events even after containment of epidemics. Children's who are infected with COVID-19 and need isolation might require special attention to meet their fear, anxiety, and psychological effect.[24]

8. Diagnosis

COVID-19 first suspected through symptoms with fever, sore throat and cough who has history of travel to china or other areas of persistent local transmission or contact with patients with similar travel history. In some patents changes in chemosensory changes like loss of smell and taste were the sign of COVID-19.[9] Some specific diagnosis is done through molecular tests on respiratory samples like throat swab, nasopharyngeal swab, sputum, endotracheal aspirates and bronchoalveolar lavage. Virus may also be detected in the stool and in severe cases the blood.[27]

Routine laboratory data in the early stage of COVID-19 epidemic are similar to common viral infection like Lymphocytopenia, prolonged prothrombin time, elevated D-dimer, liver enzymes.[1] In critical COVID-19 patients, neutrophilia, elevated D-dimer, increase in plasma blood urea nitrogen (BUN) and creatinine are also documented.[28,29] Patients admitted to the ICU will also have elevated plasma levels of the interleukins (IL-2, IL-7,IL-10). Serological markers from routine blood work were reported by comparing patients with mild or moderate symptoms to those with severe symptoms. This includes different acute phase proteins, such as SAP (Serum Amyloid Protein) and C-reactive protein(CRP).[30] Interestingly elevations in CRP appear to be unique to COVID-19 patients when compared to other viral infections.

Reverse transcriptase polymerase chain reaction (RT-PCR) assay is the first diagnostic tool used to detect COVID-19 but it is only 66-80% sensitive. This means that 20-34% of patients with COVID-19 out of 100 would test negative despite being infected. Single negative RT-PCR does not rule out COVID-19, hence a repeat RT-PCR must be performed.[12,28] Other tool is CT-chest which has 95% sensitivity in making an early diagnosis of COVID-19 through the identification of grand glass opacities. This can be intrpreted as 5 out of 100 tested will be falsely ruled out.[28] Several routine blood and serological parameters have been suggested to stratify patients who might be at higher risk for complications**.**

9. Treatment

Treatment is essentially supportive and symptomatic. The first step is to ensure adequate isolation to prevent transmission to other contacts, patients and health care workers. Mild illness with primary symptoms like fever and non-productive cough should be managed with first line antipyretic and antitussive agents. In hypoxic patients, provision of oxygen through nasal prongs, face mask, high flow nasal cannula or non-invasive ventilation is indicated.[28] Supplementary oxygen at 5 L/min must be administered for patients that require management of severe respiratory distress and oxygen saturation (Sao_2) target must be ≥92-95% in pregnant patients and ≥90% in all other patients.[28]

The severity and mortality of respiratory viral infections, including COVID-19, are associated with the host's excessive inflammatory response characterized by hyper-production of cytokines. Preclinical and clinical studies have shown that macrolides regulate the inflammatory response, attenuating the production of anti-inflammatory cytokines and also promoting the production of immunoglobulins. These regulatory effects on the immune response reduce complications of respiratory viral infections. Due to these immunomodulating properties, macrolides have been extensively study for their potential use as adjunctive broad-spectrum therapy for viral respiratory infections including influenza.[31]

According to a protocol based treatment algorithm, among hospitalized patients, use of hydroxychloroquine alone 400mg twice a day orally followed by 200mg

twice a day orally for four days would achieve therapeutic level,[32] and in combination with azithromycin was associated with a significant reduction in hospital mortality compared to not receiving hydroxychloroquine.[18] Azithromycine is also one of the drugs included in the large adaptive recovery trial, the English national study sponsored by the university of Oxort Eudract 2020-001113-21. In 2012 FDA noticed a small increase in cardiovascular deaths and deaths from any cause among patients taking azithromycine for a 5-day cycle course. It was hypothesized that Azithromycine could increase the QTc with the risk of arrhythmias. On march 2013, FDA published a communication on azithromycine safety on heart rhythms, warning on the risk of potentially fatal outcomes.[31]

Because of the potential mortality of COVID-19, National Health Commission of the people republic of china guidelines many investigational treatments are underway. Anti-viral treatment concurrent use of 3 or more antiviral agents is not recommended.[32]

Remdesivir: It is an investigational drug first developed for the treatment of Ebola. As an adenosine analogue pro drug, it putatively disrupts viral RNA transcription and is viewed as broad spectrum antiviral agent. Profoundly, remdesivir has exhibited mechanisms to overcome drug resistance and genetic mutations in coronavirus. Remdesivir is generally well tolerated with possible adverse effects of nausea, liver enzyme elevation, hypotension and respiratory failure.

Ribavirin: It is a nucleoside analog which has anti-viral avtivity against multiple RNA viruses, including respiratory syncytial virus, SARS-CoV and MERS-CoV by interfering with RNA polymerase and viral protein synthesis. Ribavirin 500mg IV 2-3 times a day for no more than 10 days. Use in combination with lopinavir / ritonavir or INF-α. The most severe adverse effects are hemolytic anemia and leukopenia. Other adverse effects include fatigue, pruritis, rash and gout. Ribavirin is a notorious teratogenic drug and is contraindicated in pregnancy.

Interferon: IFN induces several parallel antiviral pathways by triggering viral RNA degradation, RNA transcription alteration, protein synthesis inhibition and apoptosis. During the SARS and MERS outbreak interferon was widely used for its antiviral effects after showing in vitro efficacy. Interferon-α 5 million units nebulization twice a day; prepare with sterile water 2ml. The common side effects include flu- like symptoms and mood changes. It is contraindicated in patients with decompensated liver disease, severe auto immune disease, worsening psychiatric conditions, cytopenia and uncontrolled seizures.

Corticosteroids: There is evidence that severe COVID-19 patients present overwhelming inflammatory reactions with high levels of cytokines and inflammatory biomarkers, leading to lung injury. Anti-inflammatory drugs such as corticosteroids may beneficially modulate the host immune response to COVID-19 pneumonia. Corticosteroids treatment initiated as soon as the patient has shortness of breath or needs oxygen therapy, might be effective in preventing acute respiratory distress syndrome and death.[33]

Umifenovir: It is a synthetic antiviral drug marketed in Russia and China for treating seasonal influenza. It has shown broad-spectrum antiviral activity against other viruses including SARS-CoV. It is generally well tolerated. Umifenovir 200mg three times a day orally for no more than 10 days. It is used alone or in combination with other antiviral treatment in a few COVID-19.

Interleukin-6(IL-6) inhibitors: It could be a potential target for immunotherapy of COVID-19. In COVID-19 patients with cytokine release syndrome (CRS), patients were found to have elevated levels of cytokines such as IL-2 receptor, IL-6,8,10 and TNFα that indicates inflammation and immunological diseases.eg., tocilizumab 4-8mg/kg or 400mg standard dose IV once can be considered for elevated interleukin-6. May repeat a dose in 12hrs without exceeding a total dose of 800mg. side effects includes hypersensitivity reaction and infection.

The agents listed above is mostly observational in nature, with few clinical trials; and does not provide high-quality evidence. Careful consideration should be given to the numerous, clinically significant side-effects of medications that may be used in the context of COVID-19, as well as drug-drug interactions between medications, both of which may affect COVID-19 symptomology (including effects on respiratory, cardiac, immune and mental and neurological function).Currently no vaccine available for preventing COVID-19, The spike protein may serve as a vaccine candidate, but the effect to human requires further evaluation.[1] As there is no approved drug for the treatment of COVID-19, the only best way to control the spread of disease is by following guidelines of preventive measures like wearing mask, social distancing and home isolation.

10. Prevention

Currently there is no standard treatment for disease and supportive preventive measure is the only strategy. Infection preventive and control measures that may reduce the risk of exposure suggested by WHO and US centers for Disease Control (CDC) includes the following:

- Use of face mask, handgloves covering coughs and sneeze with tissue that are then safely disposed of (or if no tissues are available, use a flexed elbow to cover the cough or sneeze).[4]
- Regular hand hygiene with soap or disinfection with hand sanitizer containing at least 60% alcohol for every 15-20 min.[4,27]

- Avoidance of contact with infected people and maintain social distance of 6 feet as per recommendations of WHO.[2,4]
- Refraine from touching eyes, nose, and mouth with unwashed hands.[4]
- Proper use and disposal of mask and hand gloves, PPE is important to avoid any increase in risk of transmission.[4,34]
- Travel to outbreak areas must be prohibited.[12]
- Avoid overcrowding, particularly in public transport and public buildings.[3]
- Provide sufficient and effective ventilation, particularly in public buildings, workplace environment, schools, hospitals and aged care homes.[3]
- The virus can remain viable on surface for days in favourable atmospheric conditions but are destroyed in less than a minute by common disinfectant like sodium hypochlorite, hydrogen peroxide etc.[27]
- The public services and facilities should provide decontaminating reagents for cleaning hands on routine basis.[6]
- All healthcare workers managing COVID-19 patients require full personal protective equipment (PPE) containing surgical masks, double gloves, full-sleeved procedural gowns, and eye shield.
- The N95 masks which prevent 95% of the droplets from entering the mask must be exclusively dawned prior to performing procedures associated with a higher risk for aerosol exposure such as tracheostomy, tracheal intubation, bronchoscopy, cardiopulmonary resuscitation (CPR), and noninvasive ventilation (NIV). These procedures have the potential to aerosolize the virus.
- Containment of community transmissions is achieved by the closure of educational institutions, businesses, airspace, and sports events. High-risk individuals such as those older than 65 or having chronic comorbidities without any symptoms are also required to self-quarantine to decrease the likelihood of COVID-19 contraction.[12]
- On the development of any symptoms, the potential patient should remain quarantined in self-isolation away in a separate room with a separate bathroom for at least 14 days. This self-isolation must be extended to pets as well, as there is a recorded case of a human-to-dog transmission.[12]

Role of Vitamin C and vitamin D supplements

Vitamin C (L-ascorbic acid) has a pleiotropic physiological role, it reinforces the maintenance of the alveolar epithelial barrier and transcriptionally regulates the protein channels (CFTR, aquaporin-5, ENaC, and Na+/K+ATPase) regulating the alveolar fluid clearance. It is clear that vitamin C infusion can improve the prognosis of severe acute respiratory tract infections.[12]

Vitamin D is known to mitigate the scope of acquired immunity and regenerate endothelial lining. This may be beneficial in minimizing the alveolar damage caused in Acute Respiratory Distress Syndrome (ARDS).[12]

Vitamin B3 is highly lung protective, it should be used as soon as coughing begins. When breathing difficulty becomes apparent, hyaluronidase can be used intratracheally and at the same time 4 MU can be given to inhibit HAS 2.[5]

11. CONCLUSION

In conclusion, our study shows a holistic picture of the current epidemiological status globally in response to the outbreak of COVID-19. During this early period, many studies have been published exploring the epidemiology, causes, clinical manifestation, diagnosis, prevention and control of the novel coronavirus. Most studies have focused on the origin, epidemiology and causes. This study reviews about the status of the patients infected with COVID-19 based on their laboratory investigations. We also concluded that people with other medical comorbidities especially diabetes, immunocompromised, and elderly are at high risk of developing serious events like ICU admissions, mechanical intubation, and even death. Government agencies have quickly incorporated public policies like lockdown and home quarantine in the community, regional, and national levels to slow down and/or prevent the further spread of the COVID-19.This made people physically and mentally inactive, the WHO has issued specific psychological considerations for abating the growing stigma of COVID-19. Due to lack of vaccine and approved medications many investigational drugs are used for infected population to reduce the symptoms. As there is no effective treatment, there is continuous rise in pandemic globally. Scientists are working extensively on therapies and vaccination.

Due to lack of specific treatment we need to understand that prevention is better than cure so, we suggest the people to follow all the preventive measures that are implemented by the government and health authorities to stop the spread of disease.

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