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EPIDEMIOLOGY AND CLINICAL MANIFESTATION OF COVID 19

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Abstract

The severe acute respiratory syndrome outbreak occurred in Wuhan city, China in December 2019. The World Health Organization and International Committee on Taxonomy of Viruses termed name for the Covid-19 as severe acute respiratory syndrome Corona virus (SARS -Cov-2). It is conveyed the incubation period of this virus is 14 days and infected patient have usually fever and lower respiratory tract symptoms. Clinical symptoms appear from mild to severe and in severe condition it can lead to death. Diagnosis can be done on the basis on morphological identification of virus by electron microscopy, nasopharyngeal or oropharyngeal swabs sample collection and real time – PCR and genome sequencing. Etiological agent of this infection is corona virus; it's an enveloped (glycoprotein), lipid bilayer positive sense, single stranded RNA virus member of family corona viridae. There are seven known CoV species responsible to cause infection in human being. SARS – CoV – 2 is seventh corona virus and third known epidemic of corona virus after SARS -Cov-1 and MERS and all these three members of corona virus belong to the beta corona virus cluster. Receptor binding domain is the most mutable parts of the corona virus genome which is present in spike protein. Current studies revealed that transmission of COVID-19 in human to human occurred by respiratory droplets. There has been no proven effective current antiviral drug and vaccine available for COVID- 19. There for WHO and CDC recommend precautionary measure to overcome the spread of Covid-19 include initial diagnosis , proper reporting , isolation , basic personal hygiene like frequently hand washing ,use of surgical mask , social distancing can effectively avoid the spread of Covid-19.

Key Words: *World Health Organization , Severe Acute respiratory Syndrome , Center for Disease Control , Middle east respiratory Syndrome , Angiotensin converting enzyme , Polymerase chain reaction*

Abbreviations: *MERS: Middle East respiratory syndrome coronavirus; SARS: Severe Acute Respiratory Syndrome; ACE: Angiotensin-Converting Enzyme; RBD: Receptor Binding Domain; COVID-19: Corona Virus Disease-2019*

INTRODUCTION

The epidemic succession of acute respiratory infection with unidentified pneumonia speedily spread in China since 2019, 12 December for first the time and identified the infection associated to the source of seafood wholesale market in Wuhan and Hubei province (1). Researchers quickly identified that this is a new beta-coronavirus, 86.9% genome of which has similar to earlier distributed bat SARS-CoV genome (bat-SL-CoVZC45, MG772933.1), and discrete from human SARS-CoV and MERS-CoV (2).

The word Corona, derived from Latin word coronam which means crown, because spike glycoproteins on the surface appear crown-like structure under electronic microscope. These viruses mostly affect animals, but very less common to affect humans. The new betacoronavirus that cause acute respiratory infection with pneumonia in China termed 2019 novel coronavirus (2019-nCoV) by the WHO 12 January and on 30 January 2020, the WHO publically termed the name novel coronavirus is Corona virus Disease 2019 (COVID-19) (1). On same date, the Coronavirus Study Group (CSG) of the ICTV termed name Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). It is declared incubation period is 12-14 days and infected patients usually having fever and low respiratory tract symptoms (2).

DIVERSITY

Coronavirus is a positive- sense and single stranded RNA viruses with lipid bilayer enveloped, member of the family Coronaviridae, the Coronavirinae subfamily and the order Nidovirales and largely spread in animals (3). There are four CoVs genera alpha-CoVs, beta-CoVs, gamma-CoVs and delta-CoVs (4). Two genera alpha-CoVs and beta-CoVs are capable cause disease in mammals while the other two can effects birds and might also of infecting mammals (5). Generally, coronaviruses can survive better at $4C^{o}$ and are susceptible to heat, acidic and basic-pH (6).

There are known seven kinds of common human coronaviruses (HCoVs) which cause respiratory diseases. Among these, four are; HCoV-229E, HCoV-OC43, HCoV-NL63, and HCoV-HKU1, can lead lower respiratory infections. These HCoVs can cause severe infection in young, old or immunodeficient individuals. Since the 1960s the first two viruses, HCoV-229E and HCoV-OC43 have emerged and HCoV-NL63 in 2004 and HCoV-HKU1 in 2005. A novel beta-coronavirus came to responsiveness with identification of SARS-CoV in 2002 (7).

MERS-CoV (Middle East respiratory syndrome coronavirus) was first appeared in Saudi Arabia in 2012 (8). It was recognized as 6^{th} human coronavirus at that time and very mortal respiratory syndrome and higher mortality ratio than SARS and with reported death rate of MERS was 35.5% and SARS was 10% (9). The both betacoronaviruses, MERS-CoV and SARS-CoV can cause severe respiratory disease in lower tract in humans (10).

SARS-CoV-2, well-known seventh coronavirus and third famous epidemic of coronavirus after SARS-CoV 1 and MERS and all these three members of corona virus belong to the β-coronavirus group (5). This is a unique member of betacoronavirus, isolated from lungs epithelial cells in recent time, categorized in January by next-generation sequencing (11). This can also cause infection in lower respiratory pathway but the clinical manifestations are not serious like SARS-CoV and MERS-CoV in conformity with recent restricted confirmation reports (12).

Table I. Comparison between SARS-CoV-1 and SARS- CoV-2

Virus	Clinical presentation	Incubation Period	Mortality rate	Infection	References
SARS-CoV-1					
	Fever Dry cough Breath difficulty	2-7 days	9.6 %	More severe respiratory tract infection	Li Q et al., 2020 (13)
SARS-CoV-2					
	Fever Cough Breath difficulty	7-14 days	3.4 %	Mild severe respiratory tract infection	Huids et al., 2020 (1)

PATHOPHYSIOLOGY

The receptor binding domain (RBD) is most mutable part of coronavirus genome, present in spike protein and there are six RBD amino acid characterized for binding to ACE2 (1). Angiotensin-converting enzyme 2 (ACE2) is binding receptor for SARS-CoV-2 and binding 0f SARS-CoV 2 on ACE2 causes higher expression on type I and II alveolar epithelial cells of lungs then can damage alveolar cell. Alveolar cells damages can lead a succession of systematic reactions and even death. ACE2 expression level in alveolar cells is higher in men than women and higher level in Asian compare to white and African American populations. It is confirmed that binding capacity of SARS-CoV-2 by receptors is 10-20 times powerful than SARS-CoV -1 (11, 14).

VIRAL TRANSMISSION AND SPREAD

The first case of the CoVID-19 disease was assumed to be animal-human mechanism of transmission because it was directily linked to contact Huanan Seafood Wholesale Market of Wuhan but later cases were not linked with this exposure. Thus, current investigation resolved that transmission might possible from human-to-human**.** Current knowledge is largely derived that transmission of SARs-CoV-2 to occur from human-to-human through respiratory fomites mostly between family participants or relatives or friends who are contacted with COVID positive patients or incubation carriers (15). Symptomatic people are more contagious source for COVID-19. However, asymptomatic people could also transmit virus during the incubation period of COVID-19, expected 2 and 10 days. This is suggested that the transmission take place through coughing and sneezing droplets like other respiratory virus, containing flu and rhinovirus. Spread is also possible when contact with elevated aerosol diffusion in closed spaces. Its evidence that he spread of SARS-CoV-2 in China occur through close contact between individuals (1).

PREVENTION AND THERAPY

There are no proven active current antiviral drug and vaccines for COVID-19. Paracetamol is the first-line antipyretic therapy for fevers treatment and expectorants

(Guaifenesin) might use for cough (16). However, oxygen therapy is necessary directly for patients with severe acute respiratory infection, respiratory distress, hypoxaemia or shock

with ≥ 90% of 5 L/min to extent SpO2 in adults and children, and ≥92–95% in pregnant women (17). And intravenous fluids should be carefully directed in the absence of shock (18). It is essential to note that conventional and rational antibiotic treatments should also be directed if the patients have mild or later stages of bacterial and fungal infection. Glucocorticoids might be directed for patients with severe immune reactions and a neurominidase inhibitor such as oseltamivir for suspected infection and methylprednisolone 1–2mg/kg/day should be used in children for a maximum of 5 days (19). The National Health Commission of the People's Republic of China approvals the lopinavir or ritonavir and IFN-α treatment because these medication slower death tolls in patients infected with Severe Acute Respiratory Syndrome (SARS) (20).

In the absence of effective treatments, the WHO and US Disease Control and Prevention have serious focus on stopping spread of the SARS-CoV-2 epidemic and resist the causes of contagion. They recommend the approaches comprise initial diagnoses, isolation, and sympathetic treatments and basic personal hygiene such as frequent handwashing and use of medical facemask. However, maintenance of social orders can also effectively prevent COVID-19 infection (15).

Broad spectrum antiviral adenosine nucleotide analogue; Remdesivir (GS-5734) is a 1′-cyano-substituted fight against several RNA viruses (21) and has been identified the initial case of COVID-19 in US to treat effectively (22).

CHLOROQUINE THERAPY AND ITS MODE OF MECHANISM

Chloroquine had been used against malaria for many years and now is reported with great potential effect on COVID-19 but there is no clear evidence with a mechanism against some viral infections. It is investigated that pH-dependent phases of replication of several viruses can be possible to inhibit by chloroquine (23). It is known that chloroquine has potential broad-spectrum to inhibit virus-related disease by enhancing endosomal pH, mediated viral entry of enveloped viruses by alkalization of endosome need for cell joining and intrusive with the glycosylation of cells receptor of SARS-CoV. The mode of action depends on the inhibition of endocy-tosis or elevation of the endosomal pH. The initiative step in endosomes is the joining of endosomal membrane and viral cell at acid-pH, resulting to the genome of virus discharge into the cytosol. In other way, the virus is targeted to the lysosome at low pH with action of enzyme and interrupts the viral cell. Chloroquine restricts COVID-19 efforts to acidify lysosomes and prevents cathepsins, which need a low pH for optimum cleavage of spike protein of COVID-19 (24).

Moreover, the combination of chloroquine and remdesivir can effectively inhibit the newly emerged COVID-19 (24). Studies revealed that the actions of chloroquine gainst virus and inflammation might description for treating COVID-19 patients with pneumonia for its potent efficacy.

ASPIRIN THERAPY

A high wide-ranging produced drug aspirin could be used for the social prevention of COVID-19. Aspirin delay viral proliferation in human body but inappropriately cannot entirely block the replication of the SARS-CoV- 2. The mechanism of delay proliferation make the specific immune system stimulates to be progressively active and extend the incubation period of virus and body fights against virus better, presenting less severe symptoms. This mechanism also supports to reduce the infection on the social scale and to grow slowly in the society and avoid the transmission achieving a much less harmful infection with the increase of the asymptomatic individual. It is possible to block the most virulent expression of COVID-19 by inhibit "virus soup" phase (25).

If the replication of the virus inside the body would delay and increase the incubation time, even from 14th day onwards then the infection with increase asymptomatic and the severity of its manifestation decreases, with less patients requiring intensive care.

CONVALESCENT PLASMA THERAPY

Transfusion of convalescent plasma (CP) is convenient against pathogens, if prompts neutralizing antibodies later. The clearance of viraemia is the main action of CP therapy which usually chances after infection and typically administered after initial symptoms to maximize effectiveness (26). Several authors suggested CP as a potential therapeutic for COVID-19 pandemic (27, 28). The most critically infected patients strongly correlated with serum IL-6 levels with prolonged viremia, which consent possibility in the last stage for therapeutic intervention with antivirals and immunoglobulins (29).

Table II. Potential Antiviral drugs

Antiviral drugs	Mode of action	Mechanism	Target disease	References
Lopinavir/ Ritonavir	Inhibitor of protease enzyme	Protease Inhibitor for protein cleavage, interfere replication	SARS, MERS, HIV	32
Chloroquine	9-aminoquinolin	enhancing endosomal pH, immunomodulation,	Malaria, SARS-CoV-2	24
Remdesivir	Nucleotide analogue	stop with viral entry, genome replication	SARS,MERS, Ebola	21,33
Nafamostat	Synthetic protease inhibitor	Inhibit membrane joining by decreasing the release of cathepsin B; anticoagulant actions	MERS,Ebola, Influenza	34
Ribavirin	guanosine nucleoside analog	stop synthesis of viral mRNA capping and viral RNA synthesis	HCV,MERS,SARS	32
Oseltamivir	Neuraminidase inhibitor	Inhibiting neuraminidase enzyme which is expressed on viral surface, stopping viral replication, and infection	Influenza virus A	35
Aspirin	anticoagulant drug	Slow down proliferation of virus	SARS	25

Since day 5, in COVID-19 serum antibodies IgM and IgA appear after symptom beginning , whereas IgG since day 14 and IgG are commonly detected since day 20 (30).

Duration of antibodies for betacoronavirus immunity in plasma is 6-12 months but anti-SARS-CoV2 in plasma duration is unknown. So a suitable donor could donate 600 ml plasma (equivalent to 3 therapeutic doses) every 14 days for a minimum of 6 months (31).

CLINICAL MANIFESTATION

The clinical manifestation reported symptoms assortment from mild to severe, even severe condition can cause death. The maximum recorded symptoms were fever, cough, myalgia or fatigue, pneumonia, and complicated dyspnea, while minor common symptoms such as headache, diarrhea, hemoptysis, runny nose and phlegm producing cough was reported (12). Patient may lead to death due to damage of alveolar cells which cause progressive respiratory failure whereas with minor symptoms were recovered from virus infection after 1 week. Death tolls primarily recorded adult-patients with immune deficiency disease such as tumor surgery, cirrhosis, hypertension, coronary heart disease, diabetes and Parkinson's disease (36).

DIAGNOSIS

In China, the Viral Research Institution claimed morphology identification of the SARS-CoV-2 noticing by electron microscopy. The real-time PCR is clinical diagnosis method which mostly milestone to detect nucleic acid of COVID-19 from sample collected from nasal and throat swab and more confirmation by next-generation sequencing. And molecular assay of respiratory specimens is also used to diagnose COVID-19 at WHO-designated regional referral laboratories such as fluorescent dye. Anticipated another way to diagnose it will be available soon. Elisa, Ag, Ab direct detection can be helpful (37).

CONCLUSION AND RECOMMENDATIONS

In December, 2019 corona virus designated as Severe Acute Respiratory Syndrome (SARS -CoV-2) and cause of outbreak of respiratory ailments in a city of China, Wuhan. The WHO titled the COVID-19 abbreviated as corona virus disease 2019 .Later on World Health Organization affirmed COVID-19 as a pandemic outbreak in March.

Still no specific antiviral treatment for novel corona virus approved, only symptomatic treatment being considered and some other antiviral drugs also being tested and waiting for the trials .To overcome the threat of transmission of disease in community people and had better be instructed to wash their hands attentively cover their mouth while coughing & sneezing wear surgical Mask and avoid crowded areas. Interim World Health Organization & Center for Disease Control (CDC) has allotted guidelines .These guide lines being updated as ongoing basis of disease .We also suggest the scholar community to facilitate research to get productive results for making vaccine and drugs for novel corona virus to overcome the impact of disease all over the world .

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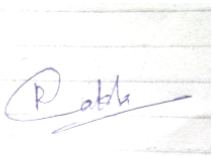
3	Rakhshanda Touheed	rakhshandatouheed@gmail.com		Conceptualized and arranged the manuscript