COVID 19: A Completely Unique Coronavirus and a Completely Unique Challenge for Critical Care

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***Abstract*- Coronaviruses (COV) are an excellent family of viruses that cause ailments starting from the cold to more severe sicknesses like Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV).2-14 days represents the present official estimated range for the novel coronavirus COVID-19.The World Health Organization (WHO) declared the 2019-20 coronavirus outbreak an epidemic and a Public Health Emergency of International Concern (PHEIC).1 The spread of coronavirus disease 2019 (COVID-19) is becoming unstoppable and has already reached the required epidemiological criteria for it to be declared an epidemic ,having infected quite 100 000 people in 100 countries.2 COVID 19 virus may be a new member of the betacoronavirus genus and is closely associated with several bat coronaviruses Compared to SARS-CoV and MERS-CoV, COVID-19 virus exhibits faster human-to-human transmission, thus resulting in the WHO declaration of a world-wide public health emergency.3 The impact of a plague depends on the amount of persons infected, the infection's transmissibility, and therefore the spectrum of clinical severity.4 On the idea of "alarming levels of spread and severity, and by the alarming levels of inaction", on March 11, 2020, the Director General of WHO characterised the COVID-19 situation as an epidemic .5**

INTRODUCTION

The fight against infectious diseases caused by viruses remains a challenging and endless task despite the tremendous efforts and significant advances publicly healthcare.[6] Novel coronavirus-induced pneumonia, which was named as coronavirus disease 2019 (COVID-19) by the WHO on the February 11, 2020, has rapidly increased in epidemic scale since it first appeared in Wuhan, China, in December 2019.According to the newest data, up to the March 1, 2020, the amount of confirmed cases in China reached 79,968, of which 2,873 were dead, and 41,681 were cured.[7] The rapid and accurate detection of coronavirus is therefore becoming increasingly important.[6] Just within the past 20 years , coronavirus have caused three epidemic diseases, namely, COVID-19, severe acute respiratory syndrome (SARS and Middle East respiratory syndrome (MERS).[7]

This virus, which is that the seventh coronavirus that has been proven to infect humans, has 75-80% genomic similarity to the severe acute respiratory syndrome coronavirus (SARS-CoV). 50% to the centre East Respiratory syndrome coronavirus (MERS-COV) and 96% to a bat coronavirus and uses an equivalent cell receptor, angiotensin-converting enzyme II (ACE2), that's employed by SARS-CoV.[8]

Coronaviruses primarily cause enzootic infection in birds and mammals and, within the last decades, have shown to be capable of infecting humans also .[9]

The purpose of this ancle is to gve people a comprehensive understanding of COVID-19, during this article the virology, the mechanism of viral infection , the treatment and diagnosis of COVID-19 are comprehensively elaborated.[10]

VIROLOGY OF COVID-19-

Coronaviruses are enveloped viruses with a positive sense single-stranded RNA genome (26e32 kb).[6] Coronaviruses, members of the Coronaviridae family and therefore the Coronavirinae subfamily are found in mammals and birds.[11] Coronaviridae consists of two subfamilies, Letovirinae and Orthocoronavirinae.[12] Coronaviruses are divided into four genera: alpha, beta, gamma and delta. The human coronaviruses HKU1 (strain named after discovery within the Hong Kong University), 7 OC43 (labeled with OC because these viruses are grown in 'Organ Culture').SARS-CoV and MERS-CoV belong to the Beta. SARS-CoV and MERS COV are genetically subgrouped into lineages B and C,

respectively. MERS-CoV genome is 30 119 nucleotides long and contains 11 open reading frames (ORFs). the only positive-stranded RNA genome has 5'- and 3'-untranslated regions that are 278 and 300 nucleotides long,respectively.[11]The coronavirus envelope characteristically contains two major viral structural proteins, the spike (S) glycoprotein and therefore the membrane (M) glycoprotein.[13]The M protein is that the most abundant structural protein and defines the form of the viral envelope.[14]

A third minor but important membrane protein is that the envelope (E) protein. E protein may be a small, 9-12 kDa integral membrane protein. The N- terminus consists of a brief 7-9 aminoalkanoic acid hydrophilic region and a 21-29 aminoalkanoic acid hydrophobic region, followed by a hydrophilic C-terminal region. E proteins play a neighborhood in viral assembly and morphogenesis.[13]MERS-CoV enters the host through its S protein, a kind I transmembrane glycoprotein with 1353 amino acids (aa) that exists on the virion surface as a trimer. 21 Subsequently, it's recognized by cluster of differentiation 26 (CD26) (also referred to as dipeptidyl peptidase 4 (DPP4)). Which facilitates the infection of the host cells 22 SARS-CoV uses angiotensin-converting enzyme 2 as a functional receptor.23 MERS-CoV and SARS-CoV differ in their cellular selection for infection, possibly due to their selective hiding with different receptors.[11]

PATHOGENESIS

It is generally accepted that the host response is liable for many of the disease manifestations in infections caused by coronaviruses. This was shown initially in mice infected with the neurotropic strains of mouse hepatitis virus (the JHMV and MHV-A59 strains).[15] Patients with COVID-19 show clinical manifestations including fever, non-productive cough, dyspnea, myalgia, fatigue, normal or decreased leukocyte count, and radiographic evidence of pneumonia, which are almost like the symptoms of SARS-CoV and MERS-CoV infections.[7]

1) Corona virus entry and replication:-

Coronavirus S protein has been reported as a big determinant of virus entry into host cells. The envelope spike glycoprotein binds to its cellular receptor, ACE2 for SARS-CoV and SARS-CoV-2, CD 209L (a C-type lectin, also called L-SIGN) for SARS-CoV. The entry of SARS-CoV into cells was initially identified to be accomplished by direct membrane fusion between the virus and cell wall . Besides membrane fusion, the clathrin-dependent and -independent endocytosis mediated SARS-CoV entry too. After the virus enters the cells, the viral RNA genome is released into the cytoplasm and is translated into two polyproteins and structural proteins, after which the viral genome begins to duplicate .[7]RNA replication is assumed to occur on double-membrane vesicles (DMVs)51). Newly synthesized genomic RNA is then incorporated into virions on membranes that are located between the endoplasmic reticulum(ER) and therefore the Golgi body (ER-Golgi intermediate compartment (ERGIC).[15]

2) Antigen Presentation in corona viral infection

While the virus enters the cells, its antigen are going to be presented to the antigen presentation cells(APC), which may be a central a part of the body's anti-viral immunity. Antigenic peptides are presented by major histocompatibility complex (MHC: or human leukocyte antigen (HLA) in humans) then recognized by virus-specific cytotoxic T lymphocytes (CTLS). Hence, the understanding of antigen presentation of SARS-CoV-2 will help our comprehension of COVID-19 pathogenesis.[7]

3) Humoral and cellular immunity

Antigen presentation subsequently stimulates the body's humoral and cellular immunity, which are mediated by virus-specific B and T cells.[7] Adoptive transfer experiments have provided insight into the mechanisms of immune protection. Adoptive transfer of CD4 T cells prevented neuronal infection. In some cases, these cells also reduced virus replication and demyelination whereas in another report, virus replication and demyelination wasn't affected. Adoptive transfer of CDS T cells resulted in protection and enhanced virus clearance.[16]

4) Cytokine storm in Covid-19

ARDS is that the common immunopathological event for SARS-CoV-2, SARS-CoV and MERS-CoV infections. one among the most mechanisms for ARDS is that the cytokine storm, the deadly uncontrolled systemic inflammatory response resulting from the discharge of huge amounts of pro-

inflammatory cytokines, and chemokines by immune effector cells in SARS-CoV infection. The cytokine storm wl trigger a violent attack by the system to the body, cause ARDS and multiple organ failure, and eventually cause death.[7]

5) Coronavirus immune evasion

The efficacy of the innate immune reaction determines the extent of initial virus replication and thus the load that the host must overcome to clear the infection. Coronaviruses, like all other successful viruses, have developed strategies to counter the innate immune reaction. IFN expression may be a crucial component of this first response, and coronaviruses have developed 'passive' and 'active tools to stop IFN induction and signalling.15 IFN-I (IFN-a and IFN-b) features a protective effect on SARS-CoV and MERS-CoV infection, but the IFN-I pathway is inhibited in infected mice.[7]

DIAGNOSIS

1) Physical examination

Patients with mild symptoms might not present positive signs. Patients in severe condition may have shortness of breath, moist rales in lungs, weakened breath sounds. Dullness in percussion, and increased or decreased tactile speech tremor etc.

2) CT imaging examination(Strong recommendation)

The maging findings vary with the patients age, immunity status, disease stage at the time of scanning, underlying diseases, are drug interventions.

Stage supported CT image:

The CT imaging demonstrates 5 stages consistent with the time of onset and therefore the response of body to the virus, including:

a. Ultra-early stage. This stage usually refers to the stage of patients without clinical manifestation, negative laboratory test but positive throat swab for 2019-nCoV within 1-2 weeks after being exposed to a virus-contaminated environment.
b. b) Early stage. This stage refers to the amount of 1-3 days after clinical manifestations (fever, cough, dry cough.
c. Rapid progression stage. This stage refers to the amount about 3-7 days after clinical manifestations started.
d. Consolidation stage. This stage refers to the amount around 7-14 days after clinical manifestations appeared.
e. Dissipation stage. This stage refers to the amount roughly between 2 and three weeks after the onset of clinical manifestations.

3) Techniques for laboratory test

Detection of pathogens in tract

a. Flu antigens: at the present, routinely detected flu antigens are A, B, and H7N-subtypes. Sampling of throat swabs is conducive to early rapid screening for flu due to the fast test, but it's a comparatively high false negative rate.
b. 2019-nCoV macromolecule detection: Accurate RNA detection of 2019-nCoV is with diagnostic value(Strong recommendation). The RNA of 2019-nCoV positive within the throat swab sampling or other tract sampling by fluorescence quantitative PCR method, especially that from multiple samples and detection kits.
c. Other laboratory testing: There are other laboratory tests for the status of 2019-nCoV infection, including blood gas analysis, liver and kidney function. Blood gas analysis is useful to guage the oxygenation of moderately-illed and severe patients. The detection of CRP and PCT is of certain value to differentiate whether there was bacterial infection within the lung. Detection of other inflammatory factors may help to preliminary evaluate the immune status of patients.[17]

4) PCR-based methods

PCR is an enzymatic method to supply numerous copies of a gene by separating the 2 strands of the DNA containing the gene segment, marking its location with a primer, and employing a DNA polymerase to assemble a replica alongside each segment and continuously copy the copies.

Owing to its large range of applications, high sensitivity and high sequence specificity, the PCR-based method has become a routine and reliable technique for detecting coronaviruses. Real-time reverse transcriptase-PCR (RT-PCR) detection is currently favored for the detection of coronavirus due to its advantages as a selected , and straightforward quantitative assay. Moreover, time RT-PCR is more sensitive than the traditional RT-PCR assay, which

help much for the diagnosis in early infection. Therefore, the real-time RT-PCR assay still may be a predominant method to be applied for the detection of all types of coronaviruses including SARS-CoV-2.[6]

CURRENT TREATMENT OF COVID-19-

Treatment principle: treat the patients to enhance the symptoms and underlying diseases, actively prevent potential complications and secondary infection; provide timely measures to support organ function.[17] SARS cases are treated symptomatically consistent with the severity of the illness. A treatment protocol consisting of antibacterial agents.[18]

1.Hypoxic respiratory failure and severe ARDS

Give oxygen therapy immediately to patients with ARDS, and closely monitor them for signs of clinical deterioration, like rapidly progressive respiratory failure. Consider severe hypoxemic respiratory failure when standard oxygen therapy fails. When patients have increased frequency of breathing (> 30 times/min) and hypoxemia even with oxygen delivered via a mask it's going to be considered as hypoxic respiratory failure. ARDS may be a status of severe acute hypoxic respiratory failure caused by increased pulmonary capillary permeability and alveolar somatic cell damage.[17]

2.Antiviral medicine treatment:-

Remdesivir was recently reported as a promising antiviral against a good array of RNA viruses. Holshue et al. for the primary time reported that treatment of a patient with COVID 19 used remdesivir and achieved good results. chloroquine has an immune-modulating activity and will effectively inhibit during this virus in vitro.[19] Chloroquine phosphate is superior to the control treatment in improving lung imaging.[20]

Remdesivir isn't expected to be largely available for treating a really sizable amount of patients during a timely manner. Therefore, of the potential drugs, CQ appears to be the drug of choice for large-scale use thanks to its availability, proven safety record, and a comparatively low cost.[19]

Hydroxychloroquine (HCQ) sulfate, a derivative of CQ, was first synthesized in 1946 and was demonstrated to be much less (-40%) toxic than CQ in animals.. More importantly, HCQ remains widely available to treat autoimmune diseases.[21]

3. Blood purification technology

Consistent with the newest studies.ACE2, the key receptor of SARS-CoV-2, is very expressed in human kidney. Kidney could be main target of attack for novel coronavirus. Early continuous blood purification treatment could reduce renal workload and help to market the recovery of renal function.

blood purification technology might be wont to remove inflammatory factors, eliminate cytokine storm, correct electrolyte imbalance, and maintain acid-base equilibrium , to regulate patient's capacity load in an efficient manner. During this logic, the patient's symptoms might be improved and therefore the blood oxygen saturation might be increased.[19]

CONCLUSION

Over the past fifty years the emergence of the various completely different corona viruses that cause an outsized sort of human and veterinary diseases has occurred. Future analysis on corona viruses can still investigate several aspects of infective agent replication and pathological process .[22] This new virus outbreak has challenged the economic, medical and public health infrastructure of China and to some extent, of other countries especially, its neighbours. Time alone will tell how the virus will impact our lives here in India.[23]Future directions for SARS-COV research include further understanding of the mechanisms of replication; elucidation of the molecular determinants of virulence and therefore the immune reaction attentively to the possible roles of group-specific proteins; development of vaccine strategies and really likely the characterization of latest pathogenic human coronaviruses.[24] The challenge now's to take care of interest in efforts to know the biology of virus and pathogenesis of disease caused by it so on minimize the danger of being surprised by its sudden reappearance.[25]

REFERENCE

[1] World Health Organization. "Novel Coronavirus (2019-nCoV): situation report, 3." (2020).

[2] Remuzzi, Andrea, and Giuseppe Remuzzi. "COVID-19 and Italy: what next?." The Lancet (2020).

[3] Gao, Yan, et al. "Structure of the RNA-dependent RNA polymerase from COVID-19 virus." Science (2020).
[4] Lipsitch, Marc, David L. Swerdlow, and Lyn Finelli. "Defining the epidemiology of Covid-19—studies needed." New England Journal of Medicine (2020).
[5] Bedford, Juliet, et al. "COVID-19: towards controlling of a pandemic." The Lancet (2020).
[6] Shen, Minzhe, et al. "Recent advances and perspectives of nucleic acid detection for coronavirus." Journal of Pharmaceutical Analysis (2020).
[7] Li, Xiaowei, et al. "Molecular immune pathogenesis and diagnosis of COVID-19." Journal of Pharmaceutical Analysis (2020).
[8] Arabi, Yaseen M., Srinivas Murthy, and Steve Webb. "COVID-19: a novel coronavirus and a novel challenge for critical care." Intensive care medicine (2020): 1-4.
[9] Zhang, Lei, and Yunhui Liu. "Potential interventions for novel coronavirus in China: a systemic review." Journal of medical virology (2020).
[10] Sun, Pengfei, et al. "Understanding of COVID-19 based on current evidence." Journal of medical virology (2020).
[11] Durai, Prasannavenkatesh, and Masaud Shah. "Middle East respiratory syndrome coronavirus: transmission, virology and therapeutic targeting to aid in outbreak control." Experimental and Molecular Medicine 47 (2015): 1-10.
[12] Banerjee, Arinjay, et al. "Bats and coronaviruses." Viruses 11.1 (2019): 41.
[13] Wilson, Lauren, et al. "SARS coronavirus E protein forms cation-selective ion channels." Virology 330.1 (2004): 322-331.
[14] Schoeman, Dewald, and Burtram C. Fielding. "Coronavirus envelope protein: current knowledge." Virology journal 16.1 (2019): 69.
[15] Perlman, Stanley, and Jason Netland. "Coronaviruses post-SARS: update on replication and pathogenesis." Nature reviews microbiology 7.6 (2009): 439-450.
[16] Perlman, Stanley. "Pathogenesis of coronavirus-induced infections." Coronaviruses and Arteriviruses. Springer, Boston, MA, 1998. 503-513.
[17] Jin, Ying-Hui, et al. "A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version)." Military Medical Research 7.1 (2020): 4.
[18] Hensley, Lisa E., et al. "Interferon-β 1a and SARS coronavirus replication." Emerging infectious diseases 10.2 (2004): 317.
[19] Wang, Li-sheng, et al. "A review of the 2019 Novel Coronavirus (COVID-19) based on current evidence." International Journal of Antimicrobial Agents (2020): 105948
[20] Gao, Jianjun, Zhenxue Tian, and Xu Yang. "Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies." Bioscience trends (2020).
[21] Liu, Jia, et al. "Hydroxychloroquine, a less toxic derivative of chloroquine, is effective in inhibiting SARS-CoV-2 infection in vitro." Cell discovery 6.1 (2020): 1-4.
[22] Geller, Chloé, Mihayl Varbanov, and Raphaël E. Duval. "Human coronaviruses: insights into environmental resistance and its influence on the development of new antiseptic strategies." Viruses 4.11 (2012): 3044-3068.
[23] Singhal, Tanu. "A review of coronavirus disease-2019 (COVID-19)." The Indian Journal of Pediatrics (2020): 1-6.
[24] Weiss, Susan R. and Sonia Navas-Martin. "Coronavirus pathogenesis and the emerging pathogen severe acute respiratory syndrome coronavirus." Microbiol. Mol. Biol. Rev. 69.4 (2005): 635-664.
[25] Satija, Namita, and Sunil K. Lal. "The molecular biology of SARS coronavirus." Annals of the New York Academy of Sciences 1102.1 (2007): 26-38.

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