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Review Article

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An updated review: The year 2020 and coronavirus disease-19 pandemic

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ABSTRACT

The recent scenario with an outbreak of novel coronavirus has led to dramatic upsurge in mortality and morbidity rates all around the globe. The objective of consolidated article is to provide an updated insight on coronavirus disease (COVID-19) based on the current literature, and it is anticipated that it may serve as a perspective reference in future studies. Scopus, Science Direct, MEDLINE, PubMed, and Google Scholar databases were used to search the literature. For the current review, both research and review articles issued in the English language were considered. The mode of Corona virus disease transmission is through direct contact or inhalation of infected respiratory droplets. The length of period of incubation varies from 2 to 14 days with maximum patients presenting mild symptoms and sign, that is, cough, fatigue, fever, and sore throat. The infection could be worst and life threatening in elderly and immuno-compromised patients. Special diagnostic molecular tests are available for detection and identification of virus. Till date, no cure is available and treatment of patients is only supportive therapy. Preventive measures such as physical isolation, hand washing, and wearing of mask should be followed. Even though, strict measures are taken into account, prevalence of COVID-19 continues to escalate worldwide and coming course of this novel virus is still not known.

Keywords: Coronavirus disease-19, Pandemic, Virus, Infection, Quarantine

INTRODUCTION

Coronavirus disease 2019 (COVID-19) was first reported in People's Republic of China (Hubei Province) but later erupted on a larger scale affecting people worldwide. With its similarity with Severe acute respiratory syndrome (SARS), it was initially catered as acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Soon after identification, the World Health Organization (WHO) titled it as COVID-19 and Emergency Committee of WHO classified it as an emergent and critical situation globally on 30th January 2020 following the grown cases not only in China but all across the globe.[1] Coronaviruses (CoVs) belong to a very diverse category of viruses which are enveloped and have single stranded RNA with a positive sense.[2] SARS-CoV-2 emerged on the world platform after it had already witnessed severe cases of acute respiratory syndrome CoV (SARS-CoV) and Middle East respiratory syndrome CoV (MERS-CoV) in 2002 and 2012, respectively. The current pandemic has brought humans to face the third induction of extreme epidemic invasion of corona virus on large-scale in the midst of the present day century.[3]

Origin wise, it is likely to be an event of zoonotic transmission coming straight from the one of the largest seafood markets, also trading in wild animals. Post identification of person to person transmission, measures are taken at wide scale to prevent the further spread whilst the current outbreak. A keen plan is observed and implied to protect the children and old, presenting themselves as the most susceptible population.[4]

The symptoms identified in most of the patients are mild, that is, fever, cough, dyspnea, and fatigue. Some of the trending presentations from confirmed COVID 19 patients include; upper respiratory tract obstruction with dyspnea,

dry cough with sputum production, a lymphopenia alongside myalgia/arthralgia, high lactate dehydrogenase, raised levels of C reactive protein and prolonged prothrombin time. In terms of severe/critical case ratio and median to intensive care admissions reported includes about 7–10% and 9.5–10.5 days, respectively. However, the mortality of 1–2% is observed with varied geographically.[5] In complete absence of suitable antiviral drugs or vaccines, with prevailing carriers and without any clear symptoms, innuendo of traditional health interventions fail to be completely effective.[6]

Further, the world is not prepared to face such a challenge and failed to learn from any of the last two epidemics of CoV as seen by the ill-preparation. The future research should bring in use the effects of the cyberspace technologies for tracing contagion. Mutual sharing of information and knowledge among various geographical locations and disciplines is the only key to combat the current situation.[7] However, various vaccines are under consideration, including; nucleic acid vaccines, viral vaccines, and recombinant protein subunit vaccines.[8] Although, the team of researchers working and aiming at the progression of a suitable vaccine against coronavirus however at the same time they are facing both logistical and scientific challenges. With this, the pressing challenge in development of vaccines remains the response of the immune system, both to pathogens and the vaccine.[9] In this time period, over 500 articles have been released in print or digital version on a weekly basis from January 13, 2020. A major portion of the article covers clinical manifestation and treatment modalities yet a great number focuses on structural elucidation, viral transmission, mechanisms/dynamics involved along with diagnostic techniques, and future antiviral treatments.[10]

With known casualties linked to COVID-19, a serious risk has been posed to the economy, triggering an ever increasing global risk and need to counter the spread. At the present time, many diagnostic kits for detection of COVID-19 are made available and have shown tremendous clinical support. In the meantime, globally institutions have stepped up with working on vaccine development, also taking it to clinical trials.[11] In this article, we aim to present a comprehensive review on COVID-19 and this review may serve as a reference for coming studies.

ONSET OF COVID-19 AND ITS EPIDEMIOLOGY

December 2019, marked an identification of a group of patients presenting pneumonia like symptoms of concealed source, initially seen in the seafood market in China (Wuhan). The unidentified disease led to blockade of human airway epithelial cells which on further investigation confirmed a novel form virus of corona family, named 2019- novel CoVs (nCoV). It belonged to subgenus sarbecovirus clade and sub-family of orthocoronavirinae. Two known variants of the same family, affecting humans were found to be different, that is MERS-CoV and SARS-CoV while 2019-nCoV stands as the seventh family member of CoVs welcoming more surveillance and investigation.[12] Phylogenetic analysis revealed its zoonotic potential along with the structural make, that is, a specific nucleic acid sequence from known human CoV (HCoVs) species, showing some similarity to that identified in bats.[13,14] Subsequent isolation from human samples followed by molecular analysis brought forth information on a new CoV, initially titled as 2019-nCoV. Following this WHO named the disease as COVID-19.[15]

To explain further, *Coronaviridae* family includes two subfamilies, that is, Torovirinae and Coronavirinae. The latter comes with a considerable number of pathogens of mammals, causing a great variety of diseases including pneumonia. Within humans, CoVs lie in a spectrum of viruses causing flu-like symptoms and majorly affecting the respiratory tract, akin to SARS and MERS, both being zoonotic in nature. While the former, Torovirinae, possess pathogens of both aquatic and terrestrial origins. Genus Torovirus entails species that is equine torovirus (Berne virus), initially isolated from a horse presenting diarrhea symptoms, while Breda virus, when isolated from neonatal calves also presented with diarrhea.[16] Further known facts include that CoVs are divided into four genera that count for α−/β−/γ−/δ-CoV. α- and β-CoV, all capable of infecting mammals, while γ- and δ-CoV are seen to cause infection in birds.[14]

Study of the incubation period presents many useful information regarding infectious diseases of respective pathogens, including tips for surveillance, control, dynamic monitoring, and modeling. For sake of active monitoring, the potentially exposed persons are required to meet the health authorities and report their health updates. An understanding of the span of vigorous monitoring is required to limit infections which is important for health departments to bring in use all limited resources.[17] Recent available evidence brings into light that approximately it takes 3–7 days for an epidemic to double in size.[18] However, more epidemiological research is needed which allows a starting point for the proceeding investigation of this outbreak and overall impact on society.[19]

In the transmission, young people may serve as asymptomatic or mildly affected individuals, contributing to silent transmission while people with a high rate of geriatric may also show impact and morbidity come mortality rates similar to that of China. Such countries include Japan, Italy, the United States and Australia. Where Australia has an elderly population of about 16% with people aged >65 years while it is 9% when compared to China. It is also important to note that there is an epidemiological similarity between the current outbreak of COVID-19 to that of SARS in 2002–2003. Prospects of limited spread still appear for Italy and Iran while open European Union may lead further transmission across Europe. This situation may also be true for countries sharing borders like Iran and its other neighbors such as Pakistan, Iraq, and Afghanistan.[20] An increased number of cases in China posed a threat to both China and others, as it exported viruses worldwide. While they managed it well with stringent policies and strengthened systems, special efforts are required for other countries, especially one possessing a high ratio of vulnerable populations. Knowledge of unascertained cases has a major contribution to continuing surveillance and interventions opted subsequently.[21]

STRUCTURE OF COVID-19

CoVs are found to be enveloped in non-segmented positive-sense RNA coming from a known family of *Coronaviridae* and

order Nidovirales. They are known for affecting humans and other mammals.[22] In terms of size, it presents a high genome size of approximately 30 kilobases. This is in harmony with other CoVs playing a part in encoding for multiple structural and non-structural proteins. HCoVs usually present a single-stranded RNA viruses consisted of positive sense. Spike (S), Envelope (E), Matrix (M), and Nucleocapsid (N) are the structural proteins [Figure 1] of this virus while non-structural proteins are RNA dependent RNA polymerase (RdRp) (nsp12). Here, RdRp acts as a crucial enzyme in the life cycle of RNA viruses and point of target in anti-viral therapies, such as Hepatitis C Virus, corona virus, and Zika Virus. In CoVs, The active site of RdRp is immensely conserved which depicts two successive aspartate residues that protrude from a beta-turn structure. It makes their surface available across the nucleotide channel where the free nucleotides can pass.[23] The protein envelope spike (S) is crucial for CoV as the S protein allows the receptor binding, mediating the membrane fusion and also deciding factor for host transmission capacity along with the tropism. Usually, the function of the S protein is divided into S1 and S2 domain, where they perform for receptor binding and serve the purpose of cell membrane fusion, respectively. It is suggested from the structure analysis that the receptor binding domain shows its composition as a core surrounded by an external sub domain. An Angiotensin converting enzyme 2 (ACE2) was believed to be a cell receptor for SARS-CoV. Just like SARS-CoV, SARS-CoV-2 also utilizes ACE2 as an entry receptor in the ACE2 expressing cells which also indicated that SARS-CoV-2 might share a similar life cycle with SARS-CoV.[24]

TRANSMISSION AND PATHOGENESIS

20th January 2020, was marked by the National Health Commission of China with a confirmed case of human-to-human transmission of the Wuhan outbreak (COVID-19).[25] The usual routes of transmission of MERS-CoV, SARS-CoV and highly pathogenic influenza were through either direct contact or spread of respiratory droplets.[26] The clinical characteristics presented in pregnant women with COVID-19 pneumonia were

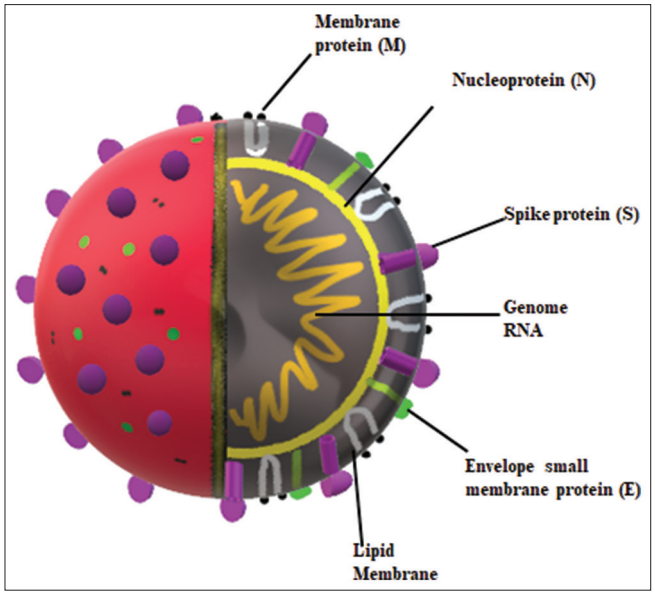

Figure 1: Structure of coronavirus disease-19

replicas of those reported in non-pregnant COVID-19 patients. The findings originating from small groups also presented the fact that no evidence is seen for intrauterine infection caused by vertical transmission among women who were developing COVID-19 pneumonia in late pregnancy.[27,28] Moreover, no evidence has brought to light the surviving capacity of SARS-CoV-2 exterior to the body for prolonged time. Although data achieved from, MERS-COV was presented with sturdiness and a considerable surviving capacity, exterior to body.[4] Thus, it can be concluded that rapid spread of COVID-19 could have originated from indirect spread through fomites, congested public places such as elevators and restrooms.[29]

Wide acceptance prevails in terms of transmission of CoVID-19 in humans and that pathogenesis mainly comes from general interactions. This includes a series of events such as virus attachment, recognition of receptor, protease cleaving followed by the involvement of S-protein (transmembrane spike glycoprotein) membrane's infusion and binding affinity of the host cellular transmembrane serine protease (TMPRSS) with COVID-19.[30] The pathogenic CoVs among human with SARS-CoV and SARS-CoV-2 has ability to bind to their target cells via ACE2. This in turn is expressed by epithelial cells of the intestine, blood vessels, lung and kidney. Expression of ACE2 is prolifically enhanced in patients with type 1 or type 2 diabetes and receiving ACE inhibitors and angiotensin II type-I receptor blockers (ARBs), for treatment purposes. The treatment of hypertension also implies ACE inhibitors and ARBs, which may cause up regulation of ACE2. ACE2 may also experience a rise by use of thiazolidinediones or ibuprofen. All this brings to consideration that the expression of ACE2 is higher in diabetics and also that treatment with ARBs and ACE inhibitors increases ACE2 expression. As a result, the infection with COVID-19 is facilitated with increased expression of ACE2.[31] ACE2 is an enzyme that physiologically counters the activation of Renin-Angiotensin-Aldosterone System (RAAS) which serves as a functional receptor to COVID-19. Data from clinical studies suggest RAAS inhibitors may raise ACE2 expression with rising concerns on safety of Covid-19 patients. However, data remain insufficient in explaining its translation among humans with no effect of study depicting the effects of RAAS inhibitors in Covid-19. Clinical trials are up taken to check for RAAS modulators, including efficacy and safety, also, use of recombinant human ARB losartan and ACE2 in Covid-19. Sudden withdrawal of RAAS inhibitors in high-risk patients, as one with myocardial infarction, may lead to unstable health and adverse outcomes. Until provision of sufficient data, one may use RAAS inhibitors in stable conditions for ones at risk with Covid-19.[32] Further, studies suggested coherence with the fact that a rise in temperature and humidity brings down the transmission of SARS and influenza, indicating that summer and rainy seasons in the northern hemisphere will considerably lessen the transmission of the COVID-19.[33]

Little study and data on MERS-CoV and SARS-CoV is a major setback. Antigen presentation consequently allows stimulation of the body's humoral and cellular immunity, run by the B and T cells. However, the antibody profile against SARS-CoV virus follows the usual pattern of Immunoglobulin M (IgM) and Immunoglobulin G (IgG) production as seen in other viral infections. The antibodies are normally produced after PRRs (pattern recognition receptors) detects PAMPs

(pathogen-associated molecular patterns) which are the microbial structures that serve as ligand for host pattern recognition. However, the major difference where SARS-CoV AND MERS-CoV deviate from this traditional approach is that they induce production of double-membrane vesicles for extensive replication, that don't possess PRRs which helps them camouflage the detection of their dsRNA by the host.[34]

SIGN AND SYMPTOMS

A wide clinical spectrum of SARS-CoV-2 infection has been witnessed worldwide. It has presented with mild respiratory infections to severe upper respiratory tract illness with pneumonia like symptoms or with respiratory failure and even death. While a large population also has been asymptomatic altogether with many hospitalized with pneumonia-like complaints as majorly found in Wuhan.[35] To elaborate, symptoms entail cough, fever, malaise, fatigue, shortness of breath and respiratory distress.[36] Moreover, frequent respiratory complaints have been registered, which has exhibited severe threats in the older and younger population, alike. This has been critical with ones presenting cardiovascular complaints.[37] Symptoms of fever, dry cough seen with COVID-19 including others like shortness of breath share commonality with previously reported SARS in 2003 and also to that of Middle East respiratory syndrome in 2012. However, the point of difference buds off from some added unique features of COVID-19 that includes incidence of diseases such as abdominal discomfort, nausea, diarrhea, and vomiting. These less frequently experienced symptoms are seen in a significant number of people with either a premature inception preceded by the conventional respirational signs.[38] With an experience of previous epidemics, corticosteroids are not recommended. This comes from the established fact that these might exacerbate COVID-19-associated lung injury and could worsen the condition.[39]

DIAGNOSIS

Epidemiological history, clinical manifestations alongside critical data originating from auxiliary examinations (like immune identification technology [Point-of-care Testing (POCT) of IgM/IgG, blood cultures], nucleic acid detection, enzyme-linked immunosorbent assay [ELISA], and computed tomography [CT] scan) serves as the main source for the diagnosis of COVID-19. It is found that the medical signs and symptoms of patients presented with SARS-CoV-2 were extremely varied and uncommon, making auxiliary examinations and epidemiological history a compulsion for prompt an accurate diagnosis of COVID-19.[34] Real-time quantitative polymerase chain reaction (RT-qPCR) and high-throughput sequencing are two most commonly used nucleic acid detection techniques implied for SARS-CoV-2.[40] It can also not be ignored that application of high-throughput sequencing technology in clinical diagnosis is limited owing to high cost and reliance on its equipment. This leaves with the option of RT-qPCR, commonly utilized with a simple and straightforward method of detection through blood and respiratory secretions.[41]

Many clinicians end up proposing CT scans with necessary auxiliary diagnostic methods to increase the sensitivity with reliable results. While patients presenting a high working hypothesis (clinical suspicion) of SARS-CoV-2 infection however false/negative screening results of RT-qPCR, bring in the need of combined and frequent RT-qPCR investigations alongside CT scan of chest. In particular, high-resolution CT for chest is a must for early diagnosis and evaluation of the severity of disease in SARS-CoV-2 patients.[42] However, with shortcomings established for currently used nucleic acid detection along with CT scans for the diagnosis of COVID-19, some immunological detection kits should be implied by the diagnostic laboratories. It helps target the viral antigens or antibodies in minimal possible time. In current times, ELISA kits and POCT of IgM/IgG have been tested and has establish advanced rate of detection than nucleic acid analysis assays yet no published list of products is available. Upon comparison.

Sensitivity of SARS-CoV S-based IgG ELISA is far less (58.9%) as compare to the results of SARS-CoV N-based IgG ELISA, that is, 94.7%.[43]

TREATMENT AND PREVENTION

The spread of COVID-19 has been rapid so far while scientists are trying day in and day out to come up with effective treatment through suitable discovery of drug or vaccine. At present, no effective treatment option is available as such, only means to boost immunity are adopted. A number of drugs, including ribavirin, interferon, corticosteroids, lopinavir-ritonavir, have been utilized in patients with SARS or MERS. Even still the efficacy of many of these drugs remains unclear.[2] Chloroquine phosphate stands out as one of the old drugs used for treatment of malaria. It has proven efficacy with reasonable safety levels against COVID-19 associated pneumonia as tested in multicenter clinical trials conducted within China.[44] Many antiviral drugs are checked for their ability of inhibiting SARS-CoV-2 replication of SARS-CoV-2 in cell culture. Among these, the drugs which have presented favorable inhibitory effects are chloroquine (CQ) and remdesivir (GS-5734). CQ holds a renowned status of effectiveness in treatment against autoimmune disease and malaria while GS-5734 is another drug which is one of the experimental drugs aimed for the treatment of infection caused by Ebola virus; the other being.[45]

Ribavirin, Remdesivir, and Sofosbuvir may be effectively utilized against the nCoV, presenting a new strain. Furthermore, the derivatives of Group Transfer Polymerization may be catered for specific inhibition of COVID-19.[23] On testing the active form (CHEMBL2016761) of Remdesivir, a perfect dock is revealed from the docking site with an overlapping region of the NTP binding motif, bringing it out as a potential therapeutic agent. However, need of clinical trials still remain for the need of confirmation of the curative effect.[46] Studies have also established the formation of antibodies against the N protein of SARS-CoV. It stands as an immunogenic protein with an immense expression in the infection and is commonly seen among viral infected patients. Besides the effectiveness of these antibodies, they have shown a shorter lifespan in the recovering individuals. Along with specific humoral immunity, responses of CD4+ and CD8+ have been found to be seen with long-lasting protection against COVID-19. The cell immunity is equally important with antibody-mediated immune response, in these infections. Peptides and epitopes

are some of the desired candidates for vaccine development as can be produced easily with little infection potential and relative chemical stability. A number of pathogenic factors and mechanisms are to be considered including above for successful vaccine formation against COVID-19.[47]

The use of serum, convalescent plasma and/or hyperimmune immunoglobulin is also found useful in treating severe acute respiratory infections of viral origin. Many of the activities including plasma donation against SARS-CoV-2, just as SARS-CoV is seen in convalescent patients.[48] Corona viral infection has turned out to be the leading hazard to not only healthcare systems, but also economies, affecting health modalities both directly and indirectly. A number of vaccines reached clinical status with the earliest Phase 1 vaccine trial tested in a synthetic DNA-based candidate. Furthermore, many new compounds plus those licensed for other conditions have been tested *in vitro* for efficacy against 2019-nCoV. Some are being tested in clinical trials against MERS-CoV and SARS-CoV, while others have been listed for clinical trials against 2019-nCoV yet no fruitful combination of individual antiviral has been proven sound for the treatment. Imperial College London published a report with respect to the stance of the UK government towards COVID-19, shifting it from "herd immunity" to more of a "pragmatic approach".[49,50] Hefty measures are implemented to cut down one to one contact hindering COVID-19 chain of transmission, especially in young and old communities.[4] To implement this classical health measures are up taken including social distancing, self-isolation, quarantine and community containment to bring to end the pandemic with underlying these respiratory symptoms.[51]

Post SARS-CoV event in 2003 calling global public health response highlights the immediate need for effective and rapid strategies of infection control. In the case of nCoV is the great potential for nosocomial transmission and risk with immune-compromised patients. Viral transmission is seen at rise due to aerosol-generation from bronchoscopy and intubation. Thus, a need of strict hospital hygiene practices is critical to prevent and control nosocomial outbreaks.[52] As per available data the close proximity between different individuals in mid of December 2019 has been massive reason for person to person transmission. Preventive measures and efforts are to be applied in regions with patients at high risk.[53] It is also rational to put on a protective face mask even especially when heading outside to prevent transmission, be it symptomatic or asymptomatic. Furthermore, the vulnerable populations should wear masks when required. In the meantime, it also is bringing in the need for research on use of masks and future production to meet mass needs.[54]

The WHO recommends the individuals who have been confirmed from laboratory as a COVID-19 patient to quarantine themselves for 14 days from the last exposed date. For implementation of quarantine, a contact person is defined as one who involved in any of the given from 2 days prior to and up to 14 days post onset of symptoms in patient: Exposed face-to-face with a COVID-19 patient within 1 meter of distance and time frame of >15 min, involved in the provision of direct care to the COVID-19 patients without implying protective garments. Residing in close vicinity to a patient infected with COVID-19 patient as in an office or home or public gathering for even the shortest of time is not sound. Moreover, travelling in close proximity is to be avoided as certain distance is mandatory in the pandemic situation. Furthermore, one should regularly disinfect surfaces coming in frequent use like bedside tables, bed frames and other furniture. It can be practiced once or twice everyday using bleach solution which has been diluted 1–99 parts of water. Otherwise 70% ethanol could be used as a substitute for bleach for surfaces that does not complement with use of 1% dilute bleach. It is important to disinfect the lavatories and its sanitary ware, at least once daily by implying domestic disinfectants or bleach. Also clothes, towels and linens should be washed with surfactant and water at 60–90°C (140–194°F) with common laundry detergent, and dry thoroughly. Disposal of waste should also be managed through sanitary landfill or any suitable method opted at the gross level to check unmonitored open areas. The personnel involved in cleaning should use gloves and protective wears when dealing in products soiled with body fluids, and they should perform disinfection and hand wash.[55]

CONCLUSION

COVID-19 is a hot issue in these days and poses a great risk to mankind health and safety. It is highly infectious and spread drastically all across the world. Till date, no treatment is available and production of vaccine is under the process. It is recommended that precautionary measures should be seriously followed to avoid infection, reduce death rates and to flatten the epidemic curve of COVID-19 virus.

CONFLICT OF INTEREST

There is no conflict of interest among the authors.

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ETHICAL CLEARANCE

Not required.

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