COVID-19: THE GLOBAL PANDEMIC WAVE – A REVIEW

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ABSTRACT

An ongoing catastrophic outbreak of a new virus tagged as nCoV-19 (Novel Corona virus-19) and currently designated as SARS-2 (Severe Acute Respiratory Syndrome), has glinted an alarm globally. Secondary infections are reportedly common in hospitalized, severely ill COVID-19 patients leading to increased mortality. The lack of natural immunity and viral replication in the lower respiratory tract lead to severe lung injury and acute respiratory distress syndrome. The anxiety and uncertainty surrounding the pandemic and the absence of antiviral drugs with complete cure are probably other contributors to the widespread prescription of antibiotics. Preventive measures such as social distancing, quarantine, prohibition of spitting in public spaces, proper hand washing, cleaning and sterilizing the surfaces are the mainstay for curbing the transmission of this virus. The present review highlights the update of novel SARS-CoV-2 in context to the Indian scenario and the superinfection and co- infections associated with COVID 19.

KEYWORDS: Covid 19, SARS-2, Super infection, Coinfection, Pandemic.

INTRODUCTION

The world is currently experiencing a widespread pandemic of Coronavirus disease 2019 (COVID19), which is imposing a deadly treat to entire human race.[1] The number has surpassed that of Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS), and is uninterruptedly rising. The outbreak which was confirmed on the New Year's Eve 2020 has now transcended the limits of various countries around the globe.[2]

The 'hotspot' for the origin of this variant of virus was initially identified in a seafood market in Wuhan, Hubei district, in Mainland China, and has gradually redeployed to Italy and to many other developing and developed countries.[2] Now USA is witnessing the maximum number of cases and fatalities every passing day followed by Brazil and India holding second and third in the line respectively.

Coronavirus disease 2019 (COVID-19) has arisen at the time of great concern on antimicrobial resistance (AMR). AMR are conventionally estimated to cause 700 000 deaths yearly worldwide and the incidence has been projected to increase to 10 million per year by 2050.[3] The number of studies specialized for COVID-19-associated superinfections or AMR is very low. Based on limited data from case series, it is reasonable to anticipate that an appreciable minority of patients with severe COVID-19 have developed superinfections, most commonly pneumonia due to nosocomial bacteria and Aspergillus.[1]

Morphology

Corona viruses are enveloped viruses carrying club shaped or crown like peplomer spikes with the appearance of solar corona. They possess linear positive sense ssRNA of 26 to 32 kbp size, largest among them are the non-segmented RNA viruses.[4]

This RNA virus, tends to mutate, due to the low proofreading ability of RNA-dependent RNA polymerase (RdRp/RP). It is found to be more potent than earlier form of SARS and MERS CoV, which has a better cultivation in human epithelial cell lines.[2]

Six varieties of corona virus have been recognised that are known to cause human infection: Human coronavirus 229E, Human coronavirus NL63 [New Haven Coronavirus], Human coronavirus OC43, Human coronavirus HKU1, SARS-CoV and MERS-CoV.

Among the six only two viruses [SARS and MERS (Middle East Respiratory Syndrome)] has been reported with an outbreak.

Epidemiology

There has been two novel corona virus outbreaks in the past 2 decades; SARS and MERS. MERS-CoV was first reported in Saudi Arabia in 2012 which caused severe lower respiratory tract illness with a mortality rate of 30%. SARS-CoV -1 was first recognised in China in 2003 by a WHO physician, Dr. Carlo Urbani, which spread from Asia to various regions of the world causing nearly 8098 cases in 29 countries with over 774 deaths.[4]

SARS -CoV-2 was first reported as a cluster of pneumonia cases in Wuhan, Hubei Province and was isolated from lower respiratory tract sample. A total of 37,604,702 people has been infected across 215 countries and 1.079,220 deaths have been attributed to this novel coronavirus, till 10 October 2020.Among the affected countries, USA holds the maximum number of active cases of 7,960,416, followed by India with 7,073,958 active cases and 108,523 deaths.[5]

Pathogenesis

The exact pathogenesis of SARS-CoV -2 is currently a mystery but most researchers believe that it might be similar to SARS due to sharing of the same receptor, ACE2. The virus initiates its virulence after adhering to the host cell by means of spike (S) glycoproteins, which further acts as a second determinant with its needs to be cleaved by host cell proteases before it can execute the fusion mechanism.

Transmission

Bats have been considered as the substantial reservoir of all coronaviruses especially SARS because they harbour a diverse range of ~3204 coronaviruses, thus prone to major host switching, thereby crafting novel coronaviruses affecting human population.[2]

Human-to-human transmission of COVID-19 was first reported in the US on January 30, 2020. [6] One- One transmission between humans occurs primarily via direct contact or through droplets spread by coughing or sneezing from an infected individual.[7]

The virus is transmitted essentially via respiratory droplets and fomites; however, recent studies have unearthed the virus lurking in the gastrointestinal tract to be transmitted via faeco– oral route.[8]

Fomite spread is of major apprehension as the virus can outlast on surfaces for a period ranging from 2 hr to 9 days. It has been noted that SARS-CoV-2 is more stable than SARS-CoV on plastic and stainless steel than on copper and cardboard.[2]

A chief impact of the unstoppable chain of transmission is by asymptomatic individuals, incessantly transmitting the infection.[9] Pre-symptomatic transmission has also been reported amongst two family clusters in China.[10]

Similar to SARS and MERS-CoV, this SARS-CoV-2 has proven as deadlier by the so-called 'super-spreading events', as were noted in SARS-CoV, but their role in the present scenario is still debatable and will be unveiled with time. Nosocomial spread has also been reported.[2] Airborne transmission of SARS-CoV-2 can occur during medical and dental procedures that generate aerosols ("aerosol generating procedures") such as cavity preparation, endodontic treatments, endotracheal intubation and extubation, non-invasive ventilation (e.g.BiPAP,CPAP) and bronchoscopy.[11,12]

Clinical presentation

The common symptoms of 2019 nCoV are fever (98%), cough (76%), dyspnoea (55%) and myalgia (44%). Rhinnorrhea and diarrhoea stays as uncommon symptoms.[14] The incubation period for this disease is 14 days, with a median of 5.1 days, and ~ 97.5% of the patients develop symptoms within 11.5 days.[2] Some positively tested cases remain asymptomatic and act as carriers.[13] The possibility of the transmission from asymptomatic carriers has been raised currently. The risk factors that were statistically significant in the progression of ARDS to mortality include older age, neutrophilia, organ and coagulation dysfunction. Patients with a fever of ≥39°C and methyl prednisolone had more chances of developing ARDS. The factors that were encountered more in the patients include dyspnoea in >59.5%, hypertension in 27.4% and diabetes in 19% and treatment with methylprednisolone.[2] The mean age for 2019-nCoV is generally between 49 and 61 years with male predominance.[14] Computerized Tomography of 56.4% of the patients showed ground-glass opacities and bilateral patchy shadows in 51.8% of patients. Many researchers have reported an elevation in the levels of ferritin, and interleukin (IL)-6. Elevated inflammatory indicators in blood, age, comorbidities. secondary infections[15] and superinfection by aspergillus have found to play a significant role in determining the fatality.[16]

Diagnosis

The identification and rapid diagnosis of infection caused by severe acute respiratory syndrome coronavirus 2 (SARS –CoV-2) is crucial to control outbreaks in the community and in hospitals. Reverse-transcription polymerase chain reaction (RT-PCR), Real-time polymerase chain reaction, RT-PCR (rRT-PCR), and reverse transcription loop-mediated isothermal amplification (RT-LAMP) are the current diagnostic test for Covid19.[17] Current diagnostic tests founded by China National Health Commission: nasopharyngeal and oropharyngeal swab tests, have become a standard assessment for diagnosis of COVID-19 infection.[18] Two one-step quantitative RT-PCR (qRT-PCR) assays were developed to detect two different regions (ORF1b and N) of the SARS-CoV-2 genome which achieves a rapid detection of 2019 n-Cov in human samples thereby allowing early identification of patients.[19] Three rRT-PCR assays targeting the RdRp/Hel, S, and N genes of

SARS-CoV-2 were developed, among these COVID-19-RdRp/Hel assay is found highly sensitive and specific and which may help in improving the laboratory diagnosis of COVID-19.[20]

SARS-CoV E gene assay found more sensitive than the two RdRp gene assays combined with the one-step RT-PCR. The E gene PCR was sufficient to diagnose a SARS-CoV-2 infection but for confirmation the RdRp protocol was recommended. Positive rate of RT-PCR detection of SARS-CoV-2 infection in 4880 cases from one hospital in Wuhan, China, was 38%.[21] Only 53.3% of COVID-19-confirmed patients had positive rate of PCR for oral swabs tests.[22] In 51 patients with confirmed COVID-19 infection, 71% patients were RT-PCR positive at the first time of testing of throat swab or sputum samples.[23] A possible shift from oral positive during early infection to anal swab positive during late infection can be observed. The RT-PCR results usually become positive after several days. Increasing automation in nucleic acid amplification testing (NAAT) with a focus on specific automated Polymerase Chain Reaction (PCR) testing can keep pace with fluctuating demand.[24] The Cobas 6800 System can help future-focused labs adjust to the changing healthcare landscape, by ushering in a revolutionary new way of thinking about nucleic acid amplification testing and was observed with good analytical performance of SARS-CoV-2 on a high-throughput platform, while offering fast and reliable results facilitating the laboratory management of large respiratory outbreaks. Shortage of commercial kits and time-consuming current laboratory test delays diagnosis.[25]

For patients suffering from fever, sore throat, fatigue, coughing or dyspnoea coupled with recent exposure, despite negative RT-PCR results COVID-19 infection should be diagnosed with chest computerized tomography (CT) characteristics.[28] Of 1014 patients, 59% had positive RT-PCR results, and 88% had positive chest CT scans.[26] COVID-19 belongs to the Coronaviridae family, therefore COVID-19 has imaging findings that are similar to those for SARS-CoV and MERS-CoV.[27] Bilateral pulmonary parenchymal ground-glass and consolidative pulmonary opacities are the typical CT findings, Sometimes rounded morphology and peripheral lung distribution also seen.[28] In chest CT scans of 21 patients, 86% of patients showed ground-glass opacities or consolidation, and more than one lobe (71%) with bilateral involvement (76%).[29] Lung cavitation, discrete pulmonary nodules, pleural effusions, and lymphadenopathy were absent. [29] Severe Lung abnormalities on chest CT scan were approximately identified 10 days after the initial onset of symptoms.[30] COVID-19 also manifests with chest CT imaging abnormalities in asymptomatic patients, with rapid evolution from focal unilateral to diffuse bilateral ground-glass opacities that progressed to or co-existed with consolidations within 1-3 weeks. Combining assessment of imaging features with clinical and laboratory findings could facilitate early diagnosis of COVID-19 pneumonia. As the diagnostic criteria expanded from laboratory examination to chest CT imaging, more than 14 000 patients were diagnosed.[31]

Superinfection and coinfection

According to the Center for Disease Control & Prevention, a superinfection is an "infection following a previous infection especially when caused by microorganisms that are resistant or have become resistant to the antibiotics used earlier," while a coinfection is an infection concurrent with the initial infection. That is, coinfections occur simultaneously, whereas superinfections develop following the initial infection. Both can add to pathogenesis, thereby increasing the morbidity and mortality due to viral infections. In respiratory viral illnesses the secondary infection most commonly involve the lower respiratory tract, and the most frequently reported pathogens include Streptococcus pneumonia, Haemophilus influenzae, and Staphylococcus aureus.

Bacterial and fungal pneumonias, especially ventilator-associated pneumonias, will likely be the most common superinfections; bloodstream infections and urinary tract infections are also seen. The use of corticosteroids, tocilizumab (anti-interleukin-6 monoclonal antibody) or other immunomodulatory agents for treatment of COVID-19 could have inadvertent outcome for secondary infections.

Through two non-mutually exclusive mechanisms Covid19 can predispose to superinfection. Hospitalized patients, especially those who are undergoing mechanical ventilation or otherwise critically ill, are at increased risk for infections, independent of SARS-CoV-2 infection.[1] Secondly susceptibility to infections may be aided by immune dysregulation coinciding with acute respiratory distress.[32]

The cause of lung pathology in patients with severe COVID-19 is due to higher pro-inflammatory (e.g., interleukin-2, soluble interleukin-2 receptor, interleukin-6, tumor necrosis factor-alpha) and anti-inflammatory cytokine (e.g., interleukin-4, interleukin-10) levels, fewer CD4 and CD8 cells, and less interferon-gamma expression by CD4 cells than those with more moderate disease Cytokine release syndrome, immune exhaustion and/or lung damage may pre-dispose to superinfection.[1]

Management

No drugs or vaccines is discovered for the condition. the symptoms are managed by use of antiretroviral drugs. Drugs used include anti-HIV drug along with anti influenza drug which proved useful against SARS this include lopinavir-ritonavir, osiltmavir. Drugs used against Ebola: Remdesivir (GS-5734), an inhibitor of the viral RNA-dependent, RNA polymerase is used in treatment of severe cases. Sarilumeb, a human monoclonal antibody which is used to treat rheumatoid

arthritis is also used in the management of inflammatory symptoms.[2]

Antimalarial drugs: chloroquine, hydroxychloroquine and antiSLE are also being used for the treatment of SARS COV -2. Ivermectin is also used which helps in reduction of the viral numbers.[33]

ACE 2 Inhibitors like losartan and telmesartan can also be used in the treatment as they do not produce cough as an adverse effect.[34]

Plasma therapy for critically ill patient for limiting the complication where the plasma of patient recovered from COVID 19 is used.[2]

Prevention
Since no perfect line of treatment is available for COVID 19, prevention is the better option where social distancing and self hygiene are the main.

Social distancing is the most effective mode and at least 6 feet of distance should be maintained from another individual. Since the disease spread through droplets mainly, use of hand hygiene measures and gloves is also very important.

WHO divided the affected cases into 4 risk categories:
High risk – individuals living in the same household of the confirmed person or caretakers, such individuals are immediately quarantined.

Medium risk- close contact with confirmed cases but with precaution.

Low risk – individuals in close contact with an asymptomatic individual.

No risk- Very small span of contact with confirmed case.[35] The COVID-19 virus spreads primarily through droplets of saliva or discharge from the nose when an infected person coughs or sneezes, so it's important that the practice respiratory etiquette (for example, by coughing into a flexed elbow) is mandatory.

Travel restriction is also needed where unnecessary travel is to be avoided. Health care workers must be prepared to handle the emergency all high-risk group must adhere to full PPE (personal protection equipment) moderate risk to N95 mask and gloves and low risk group with three layered mask and gloves. While handling the dead body of COVID 19 patient it should be placed in leak proof plastic bag decontaminated with 1% sodium hypochlorite and wrapped in mortuary sheet and then to cremation ground.[35]

Vaccines is the best preventive strategy for this disease. DNA vaccine 'INO – 4800' developed in San Diego. mRNA -1273 has given result in animal models and is undergoing open label human trials in 45 adults.[36]

Public awareness, very important for prevention, videos and posters should be circulated regarding social distancing and hand hygiene, hand hygiene should be performed thoroughly using 6 steps and alcohol-based hand rub for 20 s or with soap and water for 40 s.[2]

CONCLUSION
COVID-19 is the infectious disease caused by the most recently discovered coronavirus from the outbreak began in Wuhan, China, in December 2019. COVID-19 is now a deadly pandemic affecting many countries globally.

Most people infected with the COVID-19 virus will experience mild to moderate respiratory illness and recover without requiring special treatment. Older people, and those with underlying medical problems like cardiovascular disease, diabetes, chronic respiratory disease, and cancer are more likely to develop serious illness.

Secondary infections with bacterial, viral, and other pathogens are well-described phenomena in influenza, SARS, MERS, and other respiratory viral illnesses, data regarding superinfections/coinfections in COVID-19 pneumonia are limited and still emerging. The relatively high incidence of severe infection and mortality in COVID-19 is thought in part due to secondary infections, alongside lack of natural immunity and viral replication in the lower respiratory tract leading to severe lung injury and acute respiratory distress syndrome. Notably, there is a desire to avoid invasive diagnostic procedures such as bronchoscopy and radiologic imaging such as computed tomography (CT), in order to minimize aerosol-generating procedures and healthcare worker exposure. This has created a somewhat unique diagnostic challenge in assessing and managing secondary infections in this population relative to other respiratory viral illnesses.

The best way to prevent and slow down transmission is to be well informed about the COVID-19 virus, the disease it causes and how it spreads.

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