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A REVIEW ON CONTAGIOUSNESS OF THE NEW SARS-COV-2 VARIANT: POST IMPACT ON HOSPITALIZED PATIENTS

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ABSTRACT

SARS-CoV-2 strains evolve continuously and accumulate mutations in their genomes over the course of the pandemic. It has since rapidly become the predominant lineage, owing to high transmissibility. The severity of a SARS-CoV-2 infection could partly depend on these viral genetic characteristics. Here, we present a general conceptual framework that allows studying the effect of SARS-CoV-2 variants on COVID-19 disease severity among post hospitalized patients.

INTRODUCTION

SARS-CoV-2 evolves and new variants emerge worldwide, sustained monitoring and rapid assessment of genetic changes is required to inform the public health response and health-care management of COVID-19. Many studies have already identified older age and certain co-morbidities, such as chronic immune-compromised conditions, chronic kidney disease, cardiovascular disease, diabetes mellitus, and obesity, as risk factors for hospitalization and mortality WHO has outlined three key criteria to designate variants of concern (VOCs) in relation to global public health. COVID-19 vaccines have proven to be highly effective against laboratory-confirmed SARS-CoV-2 infections and COVID-19 hospitalizations, severe disease, and deaths. Whilst the vaccine effectiveness is shown at the population level, individual responses to vaccines will differ as a result of host factors and external factors receptors of SARS-CoV-2, such as ACE2 and TMPRSS2. COVID-19 vaccines have proven to be highly effective against laboratory-confirmed SARS-CoV-2 infections and COVID-19 hospitalizations, severe disease and deaths. Whilst the vaccine effectiveness is shown at the population level, individual responses to vaccines will differ as a result of host factors and external factors [1,2,3].

Finally, severity of a SARS-CoV-2 infection could depend on the viral genetic characteristics. For other viruses such as influenza, it is well documented that viral genetic variation plays an important role in pathogenicity. SARS-CoV-2, as other RNA viruses, evolves continuously via point mutations, deletions, insertions and possibly re-assortments resulting in an expanding phylogenetic diversity. This genetic diversity can lead to the emergence of new variants with specific characteristics. Most emerging mutations will not provide a selective advantage to the virus, in this manuscript, we present a conceptual framework that allows to study the effect of SARS-CoV-2 variants on

COVID-19 disease severity among post hospitalized patients [4,5].

Possibleness of Sars-Cov-2 Transmission from Patients

As the COVID-19 outbreak continues to evolve, we are learning more about this new virus every day. Here we summarize what has been reported about transmission of the COVID-19 virus, and provide a brief overview of available evidence on transmission from symptomatic, pre-symptomatic and asymptomatic people infected with COVID-19 [6,7].

Symptomatic transmission: Symptomatic COVID-19 case is a case that has developed signs and symptoms compatible with COVID-19 virus infection. Symptomatic transmission refers to transmission from a person while they are experiencing symptoms. COVID-19 is primarily transmitted from symptomatic people to others who are in close contact through respiratory droplets, by direct contact with infected persons, or by contact with contaminated objects and surfaces.

Pre-symptomatic transmission The incubation period for COVID-19, which is the time between exposure to the virus (becoming infected) and symptom onset, is on average 5-6 days, however can be up to 14 days. During this period, also known as the "pre-symptomatic" period, some infected persons can be contagious. Therefore, transmission from a pre-symptomatic case can occur before symptom onset.

Asymptomatic transmission An asymptomatic confirmed case is a person infected with COVID-19 who does not develop symptoms. Asymptomatic transmission refers to transmission of the virus from a person, who does not develop symptoms.

POSSIBLE DIAGNOSTIC TESTING IN COVID-19

Patients with typical clinical signs suspicious of COVID-19 such as fever, cough, sore throat, loss of taste or smell, malaise, and myalgias should be promptly tested for SARS-CoV-2. Besides symptomatic patients, patients with atypical symptoms of COVID-19 or anyone with known high-risk exposure to SARS-CoV-2 should be tested for SARS-CoV-2 infection even in the absence of symptoms [8,9,10].

❖ **Molecular Testing (RT-PCR):**

The standard diagnostic mode of testing is testing a nasopharyngeal swab for SARS-CoV-2 nucleic acid using a real-time PCR assay. Tthe qualitative detection of nucleic acid from SARS-CoV-2 from specimens obtained from nasopharyngeal swabs as well as other sites such as oropharyngeal, anterior nasal swabs, nasopharyngeal aspirates, bronchoalveolar lavage (BAL) and saliva.

❖ **Serology Testing:**

An antibody test can evaluate for the presence of antibodies that occurs as a result of infection. many commercial manufactured antibody testing kits are available to evaluate the presence of antibodies against SARS-CoV-2 are available.

❖ **Imaging Modalities:**

Considering this viral illness commonly manifests itself as pneumonia, radiological imaging has a fundamental role in the diagnostic process, management, and follow-up. Imaging studies may include chest x-ray, lung ultrasound, or chest computed tomography (CT).

- **Chest X-ray**

Standard radiographic examination (X-ray) of the chest has a low sensitivity in identifying early lung changes. In the more advanced stages of infection, the chest X-ray examination commonly shows bilateral multifocal alveolar opacities, which tend to confluence up to the complete opacity of the lung. Pleural effusion can also be demonstrated.

- **Chest Computed Tomography (CT)**

Chest computed tomography (CT), particularly high-resolution CT (HRCT), is the diagnostic method of choice in evaluating COVID-19 pneumonia, particularly when associated with disease progression.

- **Lung Ultrasound**

Ultrasonographic examination of the lung allows evaluating the progression of the disease, from a focal interstitial pattern up to a "white lung" with evidence of sub pleural consolidations. Considering its noninvasive nature and zero risks of radiation, it is a useful diagnostic modality for patient follow-up and

assists in determining the setting of mechanical ventilation and prone positioning.

❖ **Other Laboratory Assessment:**

Complete blood count (CBC), a comprehensive metabolic panel (CMP) that includes testing for renal and liver function and a coagulation panel should be performed in all hospitalized patients. Additional tests such as testing for inflammatory markers such as ESR, C-reactive protein (CRP), Ferritin, lactate de-hydrogenase (LDH), D-dimer, and procalcitonin can be considered in hospitalized patients. However, their prognostic significance in COVID-19 is not clear.

Etiology of New Sars Cov-2 : Delta Varient

Delta (21A) Variant or B.1.617.2 was first identified in India in Dec. 2020. Within a matter of months, this particular variant spread to over 98 countries around the world, becoming the dominant variant in more than a dozen of those countries including India, United Kingdom, Israel and the United States. Delta is now responsible for more than 83% of COVID-19 cases. Data indicate that it is 40-60% more transmissible than Alpha and almost twice as transmissible. where Delta accounts for ~90% of current COVID-19 cases, symptoms of Delta tend to be a little different than other strains like Fever, headache, sore throat and runny nose are common, while cough and loss of smell are not. Other reports link Delta to more serious symptoms, including hearing impairment, severe gastrointestinal issues and blood clots leading to tissue death and gangrene [11,12]. Vaccination of two doses are effective at preventing hospitalization and death, but neutralization levels of vaccinated sera are lower against the Delta variant compared to the original strain. From researchers concluded that immunity conferred by mRNA vaccines is likely to be retained against the Delta variant.

Structurally SARS-CoV-2 is similar to SARS-CoV and MERS-CoV and is composed of four main structural proteins: spike (S), envelope (E) glycoprotein, nucleocapsid (N), membrane (M) protein, along with 16 nonstructural proteins, The surface spike (S) glycoprotein, which resembles a crown, is located on the outer surface of the virion and undergoes cleavage into an amino (N)-terminal S1 subunit, which facilitates the incorporation of the virus into the host cell and a carboxyl (C)-terminal S2 subunit containing a fusion peptide, a transmembrane domain, and cytoplasmic domain is responsible for virus-cell membrane fusion. The S1 subunit is further divided into a receptor-binding domain (RBD) and N-terminal domain (NTD), which facilitates viral entry into the host cell and serves as a potential target for neutralization in response to antisera or vaccines**.** SARS-CoV-2 gains entry into the hosts' cells by binding the SARS-CoV-2 spike or S protein (S1) to the ACE2 receptors abundantly on respiratory epithelium such as type II alveolar epithelial cells. Besides the respiratory epithelium, ACE2 receptors are also expressed by other organs such as the upper esophagus, enterocytes from the ileum, myocardial cells, proximal tubular cells of the kidney, and urothelial cells of the bladder. The viral attachment process is followed by priming the spike protein S2 subunit by the host transmembrane serine protease 2 (TMPRSS2) that facilitates cell entry and subsequent viral replication endocytosis with the assembly of virions.

Post- Covid Effect on Patients Of Different Concomitent

There are some patients who have been infected with SARS-CoV-2 that causes COVID-19, have new recurring or ongoing symptoms and clinical findings seen four or more weeks after infection, sometimes after initial symptom recovery. Post-COVID conditions can occur in patients who have had varying degrees of illness during acute infection, including those who had mild or asymptomatic infections. Post-COVID conditions are being referred to by a wide range of names, including long COVID, post-acute COVID-19, long-term effects of COVID, post-acute COVID syndrome, chronic COVID, long-haul COVID, late sequelae, and others, as well as the research term Post-acute sequelae of SARS-COV-2 infection (PASC) [13,14,15,16].

Multi-organ System Effects of COVID-19

Multi-organ system effects of COVID-19 have been documented in most, if not all, body systems including cardiovascular, gastrointestinal, pulmonary, renal, dermatologic, neurologic, and psychiatric. Multisystem inflammatory syndrome (MIS) and autoimmune conditions can also occur after COVID-19. MIS can lead to longer term symptoms due to unresolved complications from the illness. The nature and duration of potential post-MIS symptoms are currently under investigation.

Cardiovascular sequelae Post-COVID:

Cardiovascular sequelae not only occur in symptomatic COVID-19 patients but have also been reported in asymptomatic patients. Up to 20%–30% of patients hospitalized with severe COVID-19 have evidence of myocardial involvement manifested by elevated troponin levels, venous thrombo-embolism, heart failure and arrhythmias. Elevated troponins in acute symptomatic patients have been associated with poor outcomes and higher in hospital mortality rates. Direct cardio-myocyte damage or damage secondary to hypoxia, microvascular dysfunction, thrombosis, and cytokine storm have been implicated. Given the high prevalence of cardiac injury, it is reasonable to expect a spectrum of heart disease with some residual post myocarditis abnormalities in severe cases. Myocardial involvement is presumed to be the initiator of inflammatory process and subsequent fibrosis (detectable on cardiac magnetic resonance imaging) and long-term sequelae too. The long-term sequelae include increased cardio-metabolic demands, myocardial fibrosis or myocardial scar, persistent left ventricular dysfunction, heart failure, arrhythmias, inappropriate sinus tachycardia and autonomic dysfunctions. Chest pain consistent with typical angina should be differentiated from atypical or non-anginal chest pain on the basis of location, aggravating and relieving factors. Likewise, respiratory causes of dyspnea need to be differentiated from cardiac causes. Heartfailure should be suspected in patients with heart disease (Pre-COVID or during acute infection)having tachycardia, neck vein distention, dyspnea, orthopnea, paroxysmal nocturnal dyspnea,pedal edema, hepatomegaly, a left ventricular third heart sound.

Gastrointestinal Sequelae Post-COVID:

SARS-CoV-2 could also be isolated from the stool samples of COVID-19 patients indicating the possibility of faeco-oral transmission. Beside the common respiratory symptoms, some COVID-19 patients experience gastrointestinal symptoms such as ageusia, lack of appetite, nausea, vomiting, dyspepsia, diarrhea, abdominal pain and hepatitis. Most symptoms pertaining to GI tract are mild and self-limiting. Presence of angiotensin converting enzyme 2 (ACE 2) receptors in the epithelium of gastrointestinal (GI) tract facilitates the entry and replication of the virus in the GI system resulting in GI manifestations. In some patients GI symptoms may appear before the onset of fever and respiratory symptoms.

Nephrological sequelae Post-COVID:

Acute Kidney Injury (AKI) is an independent predictor of mortality and poor outcomes in COVID-19 patients. COVID19 is known to cause AKI in about 46% of severe COVID-19 requiring ICU admissions. Around 20- 30% ICU patients with AKI will need renal replacement therapy. Approximately 1/3 of the COVID–19 patients with AKI, who survived will not recover kidney function to baseline values within 3 weeks after discharge from hospital. COVID-19 linked AKI also leads to faster decline in pre-existing kidney dysfunction. The prevalence of Chronic Kidney disease (CKD) among patients with recovered COVID-19 varies from 5% to 20%. Hematuria and proteinuria are found in 15% to 25% of COVID-19 patients. Few cases of COVID19 associated collapsing glomerulopathy have been reported. Signs of Post-COVID related nephrological complications: Tachycardia, Tachypnoea, hypertension or worsening hypertension, Anemia, Facial puffiness, Pedal edema.

Neurological Sequelae Post-COVID

The SARS-CoV-2 variant has a high affinity for human Angiotensin converting enzyme-2 (ACE2) receptor. This receptor is also expressed in neurons and glial cells, which could explain the reported neurological

manifestations such as olfactory neuropathy (anosmia), Peripheral neuropathy and Brain disorders. Viral particles have been found in the cerebrospinal fluid and cytoplasm of neocortex and hypothalamus neurons, as well as neuronal degeneration and necrosis, edema, glial cell hyperplasia, and cellular infiltrates. It has been suggested that in cured patients, SARSCoV-2 remains latent in the central nervous system for a long time, being able to reactivate and trigger neurological complications. Post-acute COVID–19 Neurological Symptoms includes Fatigue (most common sequelae)

- Changes in concentration
- Impaired memory Persistent muscle weakness and myalgias
- Headaches
- Sleep disorders
- Dizziness
- Impairment in smell (Anosmia) and taste (ageusia)
- Rarely new onset status epilepticus, stroke, acute inflammatory demyelinating polyneuritis(AIDP), autonomic dysfunction such as orthostatic symptoms.
- Non-specific sensory complaints such as paresthesias, numbness, tingling in limbs.

Post-chronic Covid-19 Neurological Symptoms includes

- Smell and taste disturbances
- Dysautonomia
- Headache
- Cognitive impairment
- Sleep disorders
- Neuromuscular diseases

Guillain-Barré syndrome (acute inflammatory demyelinating polyneuritis-AIDP)

- Stroke
- Epilepsy

Pulmonary Sequelae Post-COVID

The pathogenesis of SARS-CoV-2 induced pneumonia is best explained by two stages, an early and a late phase. The early phase is characterized by viral replication resulting in direct virus-mediated tissue damage, which is followed by a late phase when the infected host cells trigger an immune response with the recruitment of T lymphocytes, monocytes, and neutrophil recruitment which releases cytokines such as tumor necrosis factor-α (TNF α), granulocyte-macrophage colony-stimulating factor (GM-CSF), interleukin-1 (IL-1), interleukin-6 (IL-6),), IL-1β, IL-8, IL-12 and interferon (IFN)-γ. In severe COVID-19, the immune system's over activation results in a 'cytokine storm' characterized by the release of high levels of cytokines, especially IL-6 and TNF-α, into the circulation, causing a local and systemic inflammatory response. Besides IL-6 and TNF-α, the binding of SARS-CoV-2 to the Toll-Like Receptor (TLR) induces the release of pro-IL-1β, which is cleaved into the active mature IL-1β that mediates lung inflammation, until fibrosis**.** The persistence of respiratory symptoms and/or delayed or long-term complications of SARSCoV-2 infection beyond 4 weeks from the onset of symptoms should raise the suspicion for sequelae. If no alternate reason is found for these respiratory symptoms, the condition is termed as Long COVID. The cardinal symptoms of post-acute COVID-19 respiratory sequelae include the following

- Shortness of breath
- Dry cough
- Chest pain
- Significant sputum production
- Hemoptysis
- Ongoing breathlessness.

Dermatological Sequelae Post-COVID

COVID-19 is best known for causing fever and respiratory symptoms; it has been reported to be associated also with different extra-pulmonary manifestations including dermatological signs. COVID-19-associated cutaneous manifestations are divided in six classes (i) urticarial rash, (ii) confluent erythematous/ maculopapular/ morbilliform rash, (iii) papulo vesicular exanthem, (iv) chilblain-like acral pattern, (v) livedo reticularis/ racemosa-like pattern, (vi) purpuric “vasculitic” pattern.

Dermatological events related to COVID-19 occur due to viral infection or adverse reactions to medications used to treat it. One way to distinguish these two entities is the presence of enanthema (oral cavity lesions), which favors viral-induced eruptions. Therefore, examining the oral cavity is warranted in any COVID-19 patient with enanthema. Furthermore, the

morphology of the skin lesions caused by drug-induced eruptions include lymphocytic exocytosis, perivascular lymphohistiocytic infiltrate with or without eosinophils, interface changes (vacuolar degeneration of basal layer, apoptotic keratinocytes, exocytosis of lymphocytes), lichenoid, spongiotic, or psoriasiform changes, and papillary dermal edema. Some time the physiological impact on covid-19 cause's skin problems like Social isolation and quarantine can adversely affect many aspects of a healthy lifestyle. Stress and anxiety induced by this condition can lead to exacerbation of underlying chronic dermatoses. Examples are seborrheic dermatitis (SD) and psoriasis for which psychological factors play a significant role.

CONCLUSION

New SARS-CoV-2 infections in India are increasingly caused by the delta variant. Although the proportion of cases caused by the delta variant was 20% overall during the study period, this increased to 64% of new sequenced cases in the week starting Sep 2021.To our knowledge, this study provides the largest whole-genome-sequencing dataset for SARS-CoV-2 in a high-income country to date, enabling the assessment of hospitalization risk for the delta variant compared with the alpha variant using linked administrative data. The results suggest that patients with the delta variant had more than two times the risk of hospital admission compared with patients with the alpha variant. The possible post SARS CoV-2 effect on hospitalized patients with multi-organ impairment which leads to motility. Care clinics for post-COVID conditions are being established at medical centers across the country, bringing together multidisciplinary teams to provide a comprehensive and coordinated treatment approach to COVID-19 aftercare. This work will help to establish a more complete understanding of the natural history of SARS-CoV-2 infection and COVID-19 related illnesses, which can inform healthcare strategies, clinical decision-making, and the public health response to this virus.

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