Review Article

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Synopsis of symptoms of COVID-19 during second wave of the pandemic in India

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Abstract: COVID-19 was caused by the original coronavirus, severe acute respiratory syndrome associated coronavirus-2 (SARS CoV2), which originated in Wuhan, China. COVID-19 had a large breakout of cases in early 2020, resulting in an epidemic that turned into a pandemic. This quickly enveloped the global healthcare system. The principal testing method for COVID-19 detection, according to the WHO, is reverse transcription polymerase chain reaction (RT-PCR). Isolation of patients, quarantine, masking, social distancing, sanitizer use, and complete lockdown were all vital health-care procedures for everyone. With the 'new normal' and vaccination programmes, the number of cases and recovered patients began to rise months later. The easing of restrictions during the plateau phase resulted in a rebound of instances, which hit the people with more ferocity and vengeance towards the start of April 2021. Coronaviruses have evolved to cause respiratory, enteric, hepatic, and neurologic diseases, resulting in a wide range of diseases and symptoms such as fever, cough, myalgia or fatigue, shortness of breath, muscle ache, headache, sore throat, rhinorrhea, hemoptysis, chest pain, nausea, vomiting, diarrhea, anosmia, and ageusia. Coronavirus infections can be mild, moderate, or severe in intensity. COVID-19 pulmonary dysfunction includes lung edema, ground-glass opacities, surfactant depletion, and alveolar collapse. Patients who presented with gastrointestinal (GI) symptoms such as anorexia, nausea, vomiting, or diarrhea had a higher risk of negative outcomes. COVID-19's influence on cognitive function is one of COVID-19's long-term effects. More clinical situations need to be reviewed by healthcare professionals so that an appropriate management protocol may be developed to reduce morbidity and death in future coming third/fourth wave cases.

Keywords: COVID-19; first wave; second wave; symptoms.

Introduction

In December of this year, healthcare personnel noticed an unexplained sort of lung ailment that resulted in pneumonia due to an unknown origin. A new coronavirus was identified as the causal culprit after extensive examinations. The etiological cause for the propagation from Wuhan, China has been identified as the new coronavirus severe acute respiratory syndrome associated coronavirus-2 (SARS CoV2) [1]. Within a short amount of time, the related human sickness, coronavirus disease 2019 (COVID-19), had spread all across the world. This had reached a major explosion of instances in early 2020, resulting in an epidemic that had turned into a pandemic.

The capacity to disseminate and infect people through asymptomatic carriers resulted in a rapid and unnoticed spread all across the planet. This quickly enveloped the global healthcare system. The healthcare staffs, as well as the general public, were the hardest hit. The pandemic wreaked havoc on healthcare facilities. Critically ill patients flooded hospitals, intensive care units, and emergency rooms. To divert the flow of non-critically ill patients, makeshift hospitals, ICUs, COVID care facilities, and satellite centres were built. The WHO suggested reverse transcription polymerase chain reaction (RT-PCR) based nucleic acid amplification test (NAAT) as the principal testing method because of its accuracy and hence it remains the gold standard for COVID-19 detection. However, the technique requires laboratory settings as well as skilled personnel to conduct the test with precision. To scale up the number of tests performed per day, the need for the development of an accurate point-of-care test was of paramount importance [2].
Strict procedures such as patient isolation, quarantine, masking, social distancing, and the use of sanitizers have paved the way as health-care measures for all. These newer principles, together with a successful complete lockdown, were imposed all over the world, but they had their own consequences, resulting in economic instability all over the world, with emerging countries being the hardest hit.

The instances began to fall once the ‘new normal’ was adopted, which included stay-at-home limitations, social isolation and the use of masks, as well as the usage of sanitizers. With overworked healthcare professionals and an increase in the incidence of infections among medical employees, the only way out was to find an effective vaccination. As a result of becoming accustomed to the new normal, many companies took steps to produce a vaccine. This immunisation campaign resulted in a consistent increase in the number of recovered patients compared to those who died from the virus. According to Figure 1, the number of instances in countries like the United States has been steadily declining, while India has yet to reach a plateau. When the United States experienced a second surge in COVID-19 infection cases, India had nearly stabilised and had reached a plateau. This can be credited to the efforts of the COVID fighters, who are healthcare workers who are fighting the COVID-19 virus. Strict lockdown measures, large-scale contact tracking, isolation of positive cases, quarantine for individuals with mild symptoms, and effective treatment for symptomatic patients were all part of these efforts. This did assist us in achieving our goal of reaching a plateau period.

However, as the limits were eased during the plateau phase, cases began to resurface in early April, 2021. It wasn’t just a revival, but COVID-19 returned to the people with greater ferocity and vengeance. According to WHO, there have been 153,094,318 confirmed cases of COVID-19 worldwide as of 4 May 2021, with 3,206,339 deaths [4].

Pathogenesis

Coronaviruses are members of the Coronaviridae family and Orthocoronavirinae subfamily, order Nidovirales, and realm Riboviria [2]. Coronavirus particles are spherical, enclosed virions. From the viral membrane, cone-shaped spikes develop in a fringe-like pattern [5,6]. Coronavirus get their name from the projecting oligomers of spike glycoprotein (S) that surround the virus and form a coronal fringe. The coronavirus genome is nonsegmented, single-stranded, and RNA in the positive sense. It is in the size range of The genome also has a 5’ cap and a 3’ poly(A) tail, allowing it to function as an mRNA for replicase polyprotein translation. The nucleoprotein particles and positive stranded genome make up the ribonucleoprotein (RNP) core. A triple pass transmembrane glycoprotein (M) is present on the virus membrane and is required for virus assembly [7]. Coronaviruses have been reported to exhibit mutated and recombined behavior, producing respiratory, intestinal, hepatic, and neurologic disorders, resulting in a wide range of sickness and symptoms. The majority of its infections are asymptomatic, which has been recognised. In general, the severity of the disease is linked to underlying health issues, sex, and age (from the standpoint of the second wave). Reinfection by SARS-COV-2 is possible, however difficult to prove, according to some questionable accounts. In comparison to the initial episode of infection, the first verified case of SARS-COV-2 reinfection resulted in a less symptomatic infection, but subsequent reinfection instances may result in a more severe second infection [8,9]. According to current evidence, the membrane-bound serine protease TMPRSS2, which primes the viral S protein for fusogenic activity, facilitates SARS-CoV-2 entrance via the angiotensin-converting enzyme 2 (ACE2) receptor [10]. Because transmembrane protease serine 2 (TMPRSS2) is linked to testosterone levels, males have higher levels of expression, which could explain why they are more prone to acquire severe COVID-19 [11]. This relationship holds true for the distinction between preadolescents and adults, and it is consistent with children’s low occurrences and relatively benign disease courses [12].

Varied symptoms

COVID-19 causes a wide range of diseases and symptoms. Most infections are asymptomatic or oligosymptomatic, as

![India's Cases Rising Faster Than Others](image-url)
has been recognised. COVID-19 transmission by infected, asymptomatic persons has been recorded since the outbreak’s early stages [13,14], offering significant COVID-19 containment issues. Because asymptomatic persons do not come to health care or testing facilities, COVID-19 is most likely disseminated by them. The vagueness with which the term “asymptomatic” is employed adds to the uncertainty concerning the relevance of asymptomatic infections. A laboratory-confirmed infected person with no overt symptoms is defined as an asymptomatic case by WHO [4].

Figure 2 shows us that COVID-19 symptoms in first wave were only fever, persistent cough and anosmia with ageusia but these symptoms rapidly changed during the second wave involving conjunctivitis, skin rashes, sore throat, diarrhea, headache, fatigue and myalgia along with discoloration of finger, toes and dry mouth and tongue. Anticipating the third wave of COVID-19, it can be speculated to be having more of children being affected more along with neurological functional decline in young patients. Risk factors for severe COVID-19 infections include advanced age, medical morbidities frequently like hypertension, diabetes, obesity and smoking [15].

### General symptoms

It has been discovered in numerous current research that it takes about 5–6 days from exposure to the beginning of symptoms. However, this is not a hard and fast rule, as symptoms can emerge anywhere from three days to 13 days after exposure. As a result, COVID-19’s incubation duration is widely varied. Fever, cough, myalgia or tiredness, shortness of breath, muscle discomfort, headache, sore throat, rhinorrhea, hemoptysis, chest pain, nausea, and vomiting are among the symptoms of coronavirus infection, according to a study conducted by Nanshan Chen et al. [16]. Coronavirus infections can be mild, moderate, or severe in intensity. Some people may exhibit a combination of the symptoms listed above, while others may be asymptomatic. An early release study from China

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>COVID-19 First wave</th>
<th>COVID-19 Second wave</th>
<th>COVID-19 Query Third wave</th>
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<td>Persistent cough</td>
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<td>Neurological: Cognitive &amp; functional decline</td>
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*Figure 2: Symptoms of COVID-19 patients.*
indicated that roughly 13% of transmissions originate from asymptomatic people for many weeks in January and February. Based on currently known data and clinical understanding, a subset of people is thought to be more sensitive to COVID-19 and to be at a higher risk of serious illness. Individuals of any age with asthma (moderate to severe), chronic lung disease, diabetes, major heart diseases, chronic kidney disease requiring dialysis, extreme obesity, liver disease, an immune-compromised person, and those aged 65 and older fall into this category. Cough, trouble breathing, fever with or without chills, anosmia or ageusia, generalised body soreness (myalgia), and diarrhoea are all common symptoms according to current CDC guidelines. These symptoms can range from moderate to severe and can emerge anywhere between 2 and 14 days after being infected to the virus. Depending on skin tone, pale, grey, or blue skin, lips, or nail bed.

**Pulmonary connotations**

SARS-CoV-2 infection of ciliated bronchial epithelial cells and type-II pneumocytes causes pulmonary dysfunction in COVID-19. By attaching to the ACE2 receptor, the virus is able to enter these cells and cause viral endocytosis. The viral surface spike (S) glycoprotein is then broken by the TMPRSS2, allowing viral contents to be released and the infection to spread. Intrapulmonary shunting: The infection causes a small amount of local interstitial edema, which is focused at the interface between lung components with different elastic characteristics [17]. Alveolar collapse occurs as a result of increased lung edema (resulting in ground-glass opacities and consolidation on chest imaging), loss of surfactant, and superimposed pressure, and a significant portion of the cardiac output is perfusing non-aerated lung tissue, resulting in intrapulmonary shunting [17].

**Loss of lung perfusion regulation**

The failure of the hypoxic pulmonary vasoconstriction mechanism (constriction of small intrapulmonary arteries in response to alveolar hypoxia) during SARS-CoV-2 infection appears to be responsible for the persistence of high pulmonary blood flow to non-aerated lung alveoli, as recently demonstrated using dual-energy CT [18,19]. COVID-19 aetiology appears to be characterised by intravascular microthrombi and endothelial damage. COVID-19 [20] hypoxemia mechanisms infect lung capillary endothelial cells that express ACE2 [21,22]. In the presence of acute inflammation and endothelial damage, intravascular microthrombi are the outcome of an imbalance between procoagulant and fibrinolytic activity [23–26]. The procoagulant activity could be due to increased activity of plasminogen activator inhibitor (PAI-1 and -2), which are induced as acute-phase proteins under the influence of IL-6, or it could be due to inhibition of plasminogen activation and fibrinolysis via increased activity of plasminogen activator inhibitor (PAI-1 and -2). Diffusion capacity (DLCO) in the lungs can be reduced. Because it can detect bilateral ground glass or patchy shadowing, especially in the lower lung lobes, chest CT should be favored over normal chest X-rays in the vast majority of patients.

**Cardiovascular**

Direct myocardial injury: viral entrance could disrupt the ACE2 signalling pathways, resulting in acute myocardial injury. Acute systemic inflammatory response and cytokine storm are two of the most serious side effects of the virus. Multi-organ failure may result from these modifications. High levels of circulating cytokines are found in the clinical labs of seriously unwell patients. Increased sickness due to a change in the myocardial demand-supply ratio Cardiometabolic demand induced by systemic infection, along with hypoxia induced by severe respiratory sickness, might compromise the myocardial oxygen demand-supply connection, resulting in acute myocardial damage [27]. Arrhythmias: both tachy and bradycardia are seen in COVID-19 infection.

**Hypercoagulable states**

Hypercoagulability is a known complication of SARS-CoV-2 infections [28]. Patients infected with COVID-19 had a significant rate of pulmonary thrombosis (up to 79%) [28]. Thrombosis was observed in 31–79% of COVID 19 patients in investigations conducted in intensive care units [28,29]. Severe thrombosis occurs in critically ill COVID 19 patients due to increased pro-inflammatory and anti-fibrinolytic alterations in circulation. Zhou et al. identified significant lymphopenia, increased D-dimer, lactic dehydrogenase, and IL-6 levels in 54 COVID-19 infected patients who died from the disease [30]. COVID-19 infections aggravated by coagulopathy are characterised by elevated D-Dimer levels.

**GIT**

GI symptoms were present in the majority of COVID-19 patients, and they were linked to a greater rate of negative
outcomes including ICU hospitalisation and/or fatality. Anorexia and diarrhoea were the most common gastrointestinal symptoms, followed by nausea and vomiting, nausea and vomiting, and abdominal discomfort in a small percentage of cases. In China, patients in Hubei Province had significantly greater rates of nausea, vomiting, and diarrhoea than those in other provinces [31]. Pediatrics was more likely than adults to experience abdominal pain, nausea, or vomiting. Gastrointestinal damage was more common among female and elderly individuals. For SARS-CoV-2 to penetrate host cells, the ACE2 receptor is essential. SARS-CoV-2 enters the digestive tract directly through binding to ACE2 receptors in gastric glandular cells, duodenal and rectal epithelial cells, and small intestinal enterocytes. Furthermore, after infection with SARS-CoV-2, the “gut-lung” axis, as well as the interplay between intestinal microbiota and pro-inflammatory cytokines, may cause gastrointestinal tract harm [32].

Skin

COVID-19 has recently been linked to novel dermatological symptoms on the skin, which occur alongside other frequent symptoms such as fever and dry cough. Several COVID-19 patients have recently complained severe itchy hives and rashes, while others have claimed a burning feeling on their skin. The formation of pseudo-frostbite of the extremities, the appearance of painful and persistent redness, and transient, hive-like lesions are all indicators of skin lesions, according to the French dermatology union, Le Syndicat National des Dermatologues-Vénérologues (SNDV). These symptoms may be linked to COVID-19, according to an analysis of a number of cases reported to the SNDV. Rashes of all sizes and shapes have formed all over the body. All regions of the body were impacted by dermatological eruptions or inflammation, with the trunk being the most severely affected. There was also some modest cutaneous scarring [33].

Conjecture of the third wave of COVID-19

Spheres of risk factors and presentation of symptoms seen in different waves of COVID-19 pandemic (Figure 3). COVID-19’s influence on cognitive function, even in persons with modest symptoms, is one long-term effect that is becoming increasingly obvious. One-third of COVID-19 patients experience neurological symptoms, including anecdotal reports of ‘COVID-19 delirium’, which manifests as paranoid hallucinations, disorientation, and agitation in over 20% of hospitalised patients [34,35]. Patients over 65 years of age are one of the most vulnerable groups for severe COVID-19 symptoms, as they frequently have underlying moderate cognitive impairment and are already at risk of delirium due to underlying ‘neurocognitive frailty’ [36,37]. COVID-19-related inflammation raises the risk of silent infarcts, permeability of the blood-brain barrier (BBB), thrombosis, and coagulopathy, all of which can exacerbate neurological damage [38]. Taken together, there’s mounting evidence that a patient’s COVID-19 risk factors, pathology, and treatment course can all contribute to long-term cognitive and functional deterioration, both separately and synergistically (Figure 4).

The significant agitation associated with delirium in many COVID-19 patients in the ICU presents difficulties for staff and adds to the stress of caring for these critically ill patients. Long-term investigations on COVID-19 survivors have yet to be completed, but short- and medium-term neurological impairments have already been found in both critically ill and non-critically ill survivors. In fact, disorientation or altered awareness is the fourth most prevalent presenting symptom of COVID-19, implying both direct and indirect early neurological effects. Because cognitive decline is usually an insidious process following a major neurological or neurocognitive trauma, our findings raise serious concerns about the continuing development of cognitive and functional decline in these patients. Furthermore, cognitive decline does not occur in isolation; rather, it is accompanied by a decline in quality of life and an inability to conduct both routine and instrumental activities of daily living (ADLs) (IADLs). Cognitive decline is frequently misdiagnosed until it has progressed to the point where it is associated with moderate to severe functional difficulties.

Conclusions

In India, pathological virulence is substantially more severe, resulting in a high fatality rate. More clinical conditions should be examined by healthcare experts monitoring cases so that an appropriate management protocol may be created to prevent morbidity and mortality, as well as the likelihood of a future developing third and fourth wave due to the virus’s rapid mutations. Whether this saga of suffering and pain caused by the loss of loved ones in the community will come to an end soon is a question that has yet to be answered.
Figure 3: Spheres of risk factors and presentation of symptoms seen in different waves of COVID-19 pandemic.

Figure 4: Wheel of factors contributing to long-term cognitive and functional decline [15].
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References


