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CLINICAL MANIFESTATIONS OF COVID-19: A NARRATIVE REVIEW

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ABSTRACT
The clinical manifestations of COVID-19, caused by the SARS-CoV-2 virus, exhibit a broad spectrum of symptoms ranging from asymptomatic or mild respiratory illness to severe pneumonia, acute respiratory distress syndrome (ARDS), multi-organ failure, and death. The incubation period typically ranges from 2 to 14 days, with a median of 4 to 5 days. Early symptoms often include fever, cough, and fatigue. Other common manifestations include dyspnea, myalgia, sore throat, and headache. Gastrointestinal symptoms, such as diarrhea, nausea, and vomiting, are also reported in some cases.
Severe cases may progress to respiratory distress, requiring oxygen therapy and mechanical ventilation. Hypoxemia and respiratory failure are critical indicators of severe disease. The disease can also precipitate a hyperinflammatory response, leading to complications such as cytokine

storm, which exacerbates lung injury and can lead to systemic inflammation affecting the heart, kidneys, and liver. Cardiovascular manifestations include myocarditis, arrhythmias, and acute cardiac injury. Coagulopathy, characterized by elevated D-dimer levels and thrombosis, is a significant concern, increasing the risk of venous thromboembolism and stroke.

Neurological symptoms range from anosmia and ageusia to more severe conditions such as encephalopathy, seizures, and Guillain-Barré syndrome. Skin manifestations, including rashes, urticaria, and "COVID toes" (chilblain-like lesions), have been observed. The severity and range of symptoms vary widely, influenced by factors such as age, comorbidities, and immune response. Older adults and those with underlying conditions like hypertension, diabetes, and obesity are at higher risk for severe disease and mortality.

Understanding the diverse clinical manifestations of COVID-19 is crucial for timely diagnosis, management, and therapeutic intervention. Continuous research is necessary to unravel the pathophysiological mechanisms underlying these manifestations and to develop effective treatment strategies.

Keywords: clinical manifestations, COVID,

INTRODUCTION

World Health Organization (WHO) declared a global pandemic in March 2020 due toWuhan, China, which first reported novel virus presence in 2019 (December) that was identified as severe acute respiratory coronavirus 2 (SARS-CoV-2). (1). One factor that could contribute to a higher degree of illness severity is the co-occurrence of respiratory infections (2). Within 48 hours (about 2 days) of COVID-19 diagnosis, patients of all ages and COVID-19 severity levels who underwent screening for respiratory virus co-infection (3). In individuals who are hospitalized or not, COVID-19 is linked to a few neurologic symptoms, including autonomic ones (4, 5). Fever, dry cough, weakness, and trouble breathing are chief symptoms of SARS-CoV-2 infection. There have been reports of abnormal liver function tests; approximately 50% of patients have abnormal liver tests to varying degrees (6-7). Physicians can treat patients more effectively and control infections by using data on co-infecting virus prevalence and most prevalent types. When proper, they can also treat patients with suitable antiviral medication. To figure out the prognosis of a patient, it is critical to understand the risk factors for co-infection and any potential alterations to the disease's clinical course (8).

TRANSMISSION DYNAMICS:

Before animal-to-human transmission without regard to animal species was thought to be the cause of the infection (9, 10).Later, as more people with the disease without a history of market exposure were being diagnosed, it was determined transmission via human-to-human contact is, in fact, a prevalent mechanism of viral propagation (11-12). Numerous species are known to harbor coronaviruses (13). The most hazardous of these carriers are rhinolophid bats, who don't show any outward symptoms of infection (14). When the virus infects other species, it can cause catastrophic illnesses like infectious bronchitis (IB) in chickens, which might cause the poultry sector to suffer significant financial losses (15).

GEOGRAPHICAL DISTRIBUTION:

COVID-19 spread quickly after being first reportedin China and frequency of cases spiked dramatically. China was followed by Thailand that reported first case on January 11 (16). On February 26, 2020, COVID-19, a new and poorly understood disease, was found to have its first case in Pakistan. Having little resources, a deteriorating healthcare system, and poor health spending, as a developing nation (17), Pakistan is very susceptible to communicable diseases and has never had a pandemic (18). By February 23, 2022, 43% of the nation's population had received all recommended vaccinations (19), with the Omicron strain of COVID-19 being the most common strain (20).

RESPIRATORY SYMPTOMS & COMPLICATIONS:

High short-term morbidity and mortality have been linked to the COVID-19 pandemic. The primary organ impacted by an infection with SARS-CoV-2 is lung. Long-term COVID-19-related pulmonary sequelae are predicted to increase dramatically, having a longer-lasting effect on community health and healthcare systems. There have been many other long-term respiratory issues linked to COVID-19 that have been reported, including lung fibrosis, poor respiratory physiology, vascular problems, and persistent symptoms and radiologically noticeable changes (21).

COMMON SYMPTOMS:

Individuals with COVID-19 may have varying symptoms. After exposure, symptoms often start 5-7 days later and continue 11-14 days.

Cough, fever, and chills are characteristic symptoms. Less frequently observed symptoms include sore eyes, headaches, tightness in the chest or chest pain, dizziness, shortness of breath, appetite loss, hoarse voice, nausea, vomiting,trouble sleeping, abdominal pain or diarrhea, loss or alteration of sense of taste or smell and numbness or tingling. Muscle aches and heavy arms or legs are also common symptoms (22).

RISK FACTORS:

When COVID-19 is diagnosed, those havingany existing medical condition are more vulnerable and should seek medical attention as soon as possible. Those on immunosuppressive medications, those with HIV, diabetes, cancer, or chronic heart, lung, or liver issues, or those with rheumatological issues are among them. dementia or obesity (23).

CLINICAL MANIFESTATIONS:

A retrospective observational study conducted in Sudan between the 1st of April and 30th of September 2020 done todetermine clinical findings and patientsoutcomeshaving COVID 19.The study included 243 patients. Male to female ratio was 145:98 and mean age was 55.8.Commonest general manifestations was fever followed by fatigue while commonest pulmonary manifestations was Cough followed by shortness of breath.Critical patients diagnosed with COVID-19 showed a higher rate of mortality,Old age was also associated with mortality (24).

A study conducted in China between the between 30 December 2019 and 29 February 2020 done todeterminefeatures and prognostic factors of COVID-19. The study design was retrospective study with a sample size of 293 patients. Male to female ratio was 138:155.Ratio of surviving to non-surviving was 177:116.Fever was the most common complications followed by Cough and weakness. On surviving groups showed a higher rate of lymphopenia, Leukocytosis, and neutrophilia,Old age was also associated with non-surviving group (25).

A study conducted in China between the between January 9, 2020, and February 15, 2020 reported clinical findings of 85 fatal COVID-19 cases in Wuhan.Study design was retrospective study with a sample size of 85 patients.Male to female ratio was 62:23 and mean age was 65.8.Commonest symptoms was Fever followed by shortness of breath,fatigue and dyspnea.Multiple organ failure was most commonly associated with death.Mortality was high among patients of age 50 or above (26).

A study carried out in China from January 10 to March 15, 2020, sought to characterize COVID-19 patient features and variables linked to a severe or critically sick presentation.A multicenter retrospective cohort study with a 625-patient sample size was the study's design.The mean age was 44.44 and the male to female ratio was 329:296.Fever was the most frequent symptom, followed by cough and sputum.Severe patients had a history of diabetes and hypertension; they also had lower albumin, white blood cell, lymphocyte, and platelet counts; higher temperature,

faster breathing rates, lower peripheral capillary oxygen saturation (SpO2), higher computer tomography (CT) image quadrant scores, and higher pulmonary opacity percentage; upon admission, they also had higher levels of fibrinogen, D-dimer, and C-reactive protein.Older people had a higher ratio of seriously ill patients (27).

A study conducted in China,aimed to discover risk factors and clinical features of Mortality for COVID 19 patients and formulate a extensive risk model evaluating the death risk of COVID-19.The study design was retrospective observational study with a sample size of 993 patients.Male to female ratio was 655:338 and mean age was 68. Fever was the most common symptom followed by cough,dyspnea and expectoration. A higher COVID-19 death risk was associated with higher SOFA, qSOFA, APACHE II and SIRS scores, hypoxia, elevated inflammatory cytokines, multi-organ dysfunction, decreased immune cell subsets, and complications (28).

A study conducted in Japan aimed to investigate the characteristics, inflammatory laboratory finding trends, and outcomes among critically ill patients.The study design was retrospective observational study with a sample size of 24 patients.Male to female ratio was 19:5 and mean age was 57.5.Commonest symptom was fever followed by Dyspnea.High neutrophil compared to normal was seen among patients.Mortality rate was low,Survivors needed ventilation but letter discontinued (29).

A study conducted in Indonesiaaimed to report the characteristics of COVID-19 patients in Bali, Indonesia, and evaluates the diagnostic value of their clinical symptoms .The study design was observational with a sample size of 92 patients.Male to female ratio was 53:19 and mean age was 50.8.Commonest general manifestations was fever followed by fatigue while commonest pulmonary manifestations was Cough followed by shortness of breath.Severe and critically ill patients diagnosed with COVID-19 showed a higher rate of mortality,Old age was also associated with mortality (30).

A study (case report) has been conducted in Sakraya,Turkey that highlights four cases of COVID-19 patients diagnosed simultaneously with acute ischemic stroke. The patients, aged between 45 and 77 years, exhibited typical COVID-19 symptoms and were likely infected locally. Elevated D-dimer and CRP levels suggested increased inflammation, potentially contributing to ischemia. The findings emphasize the need to consider cerebrovascular events in COVID-19 patients, particularly in older individuals with prothrombotic risk factors, alongside infectious symptoms (31).

The severe instances of COVID-19 have lower platelet counts, shorter activated partial thromboplastin times, higher levels of D-dimer and fibrinogen, and longer prothrombin times, according to a meta-analysis of 34 studies involving 6492 individuals. In comparison to survivors, patients who passed away showed noticeably greater D-dimer levels, longer prothrombin times, and lower platelet counts. These results imply that coagulation dysfunction is associated with the severity of the disease and is common in severe COVID-19 cases (32).

A meta-analysis of 16 articles includes number of patients from 34 to 1263, the age of patients varied from 15 to 43 years with a mean of 38.52. It examined anosmia prevalence among COVID-19 patients in India from Jan 2020 to Mar 2021, finding it varied widely, from 9.2% to 82%, averaging 30.19%. Objective tests like UPIST or SNIFFING STICK showed a cumulative incidence of 52.2%, while subjective analysis yielded 16.4%. This underscores the need for reliable objective tests due to the lack of a globally accepted standard for smell assessment, similar to vision and hearing exams (33).

In a study on 284 COVID-19 patients, conducted from May 1, 2020, to June 25, 2020, the median age was 48 years, with 33.80% being female. Symptoms included fever (85.56%), shortness of breath (49.65%), cough (45.42%), and headache (40.86%). Patients with multiple comorbidities, particularly diabetes and smoking, tended to present as severe-critical cases in comparison to healthy patients, diabetics, and smokers alone. Smokers had a lower mortality rate in comparison to diabetic patients and those with both diabetes and smoking. While smokers had higher death rate compared with healthy cases, they were lower than that of diabetic patients and diabetic plus smoker patients (34).

A systemic review and meta-analysis was done on COVID-19 neurological and musculoskeletal symptoms. 61 studies included in review and 51 studies in meta-analysis. The mean range from 24-95 years, focusing on headache, dizziness, loss of taste and smell, myalgia, back pain, muscle weakness, and other symptoms. These symptoms, which range in incidence from 1% to 35%, can appear before or with more frequently recognised symptoms like as fever and cough. Understanding and identifying these signs is critical for early identification, prevention, and treatment planning (35).

A systematic review and meta-analysis was conducted on clinical symptoms of COVID-19. 54 articles were included. It concludes that fever (81.2%) was the most prevalent symptom, followed by cough(58.5%), fatigue(38.5%), dyspnea(26.1%), and sputum production(25.8%). Interestingly, the sample size of the studies didn't significantly affect the final estimates. Recognizing these symptoms early can aid in the prompt detection and containment of the disease (36).

A meta-analysis of 31 articles involving 46,959 COVID-19 patients reveals key clinical and imaging features. Common symptoms include fever (87.3%), cough (58.1%), and dyspnea (38.3%), with bilateral pneumonia (75.7%) and ground-glass opacification (69.9%) prominent in imaging. Approximately 29.3% require ICU admission, with a case fatality rate of 6.8%. COVID-19 poses significant respiratory risks, often leading to rapid lung function deterioration and potential mortality (37).

The study aimed to estimate the prevalence and recovery rates of anosmia (loss of smell) and ageusia (loss of taste) in COVID-19 patients. Conducted from June to September 2020 at a dedicated COVID-19 hospital, it included 200 patients aged 12-70 years with mild to moderate symptoms confirmed by reverse transcriptase polymerase chain reaction (RT-PCR). Using the DyNaCHRON (Dysfonctionnement Nasal Chronique = Chronic Nasal dysfunction) questionnaire, the prevalence of isolated ageusia was found to be 7%, isolated anosmia 4.5%, and combined anosmia and ageusia 4%. Ageusia typically resolved within 14 days, while anosmia, with or without ageusia, resolved within 21 days for most patients, except for two who experienced long-term anosmia. Early screening for these symptoms can aid in the timely diagnosis and treatment of COVID-19 (38).

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