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"Exploring the Clinical and Laboratory Aspects of Novel Coronavirus Infection (COVID-19): A Systematic Review"

Researchers:

Mohammad Ali Yahya Sharefe,[1] Abdullah Hussain Ali Alshahrani,[2] Zayed Ahmed Zayed Asiri,[3] Sultan Hamoud Mohammed Albaqami,[4] Yasir Saad Saeed Al Shalan,[5] Mohammed Maeed S Alqahtani,[6]

1. Specialist-Emergency Medical Services,Profile No: 18AA0004026, Armed Forces Hospital Southern Region,Saudi Arabia.
2. Pharmacist-Pharmacy,Profile NO : 16RP0024918, Prince Sultan Military Medical City,Saudi Arabia.
3. Technician-ursing,Profile No: 08RN0031893, Armed Forces hospital southern region,Saudi Arabia.
4. Technician-Preventive Health,Profile NO : 14RN0040609, King Fahd Armed Forces Hospital,Saudi Arabia.
5. Pharmacist-Pharmacy,Profile NO : 15AP0018746, Armed Forces hospital southern region,Saudi Arabia.
6. Pharmacist-Pharmacy,Profile NO : 18AP0031702, Armed Forces hospital southern region,Saudi Arabia.

CONTEXT:

The COVID-19 pandemic, caused by the novel coronavirus SARS-CoV-2, has resulted in significant morbidity and mortality worldwide. Understanding the clinical and laboratory aspects of this virus is crucial for effective diagnosis and management, especially among vulnerable populations.

OBJECTIVES:

The objective of this systematic review is to explore the clinical and laboratory characteristics associated with COVID-19, specifically focusing on the diagnostic methods, laboratory findings, and implications for patient management.

METHOD:

To acquire pertinent information, we conducted an extensive electronic search across reputable databases including Google Scholar, Scopus, Medline, and PubMed, spanning from January 2024 to April 2023.

RESULTS:

The review indicates that COVID-19 presents with a range of symptoms from asymptomatic cases to severe respiratory distress. Key laboratory findings include elevated levels of inflammatory markers such as C-reactive protein (CRP) and alterations in leukocyte counts. The use of RT-PCR testing for viral RNA is essential for diagnosis during the early symptomatic phase.

CONCLUSION:

Laboratory diagnostics play a pivotal role in understanding COVID-19. Proper interpretation of laboratory markers can enhance patient management, facilitate the identification of asymptomatic carriers, and improve monitoring of symptoms. Ongoing research is necessary to refine diagnostic methods and address remaining uncertainties regarding long-term immunity.

KEYWORDS:

COVID-19; SARS-CoV-2; immunological assays; reverse transcriptase-polymerase chain reaction; biomarkers; clinical pathology.

ABSTRACT :

COVID-19 is a highly transmissible illness caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The World Health Organization (WHO) declared it a pandemic in 2020, following its rapid global spread. While the virus can lead to severe illness, particularly among vulnerable groups such as the elderly, individuals with compromised immune systems, diabetics, those with heart conditions, and patients with hypertension, many infected individuals remain asymptomatic or exhibit mild to moderate respiratory symptoms. The most critical manifestation of COVID-19 is often marked by a cytokine storm (A cytokine storm : is an intense immune response marked by the excessive release of pro-inflammatory cytokines into the bloodstream. This can cause widespread inflammation and tissue damage across multiple organs. Commonly linked to severe infections, autoimmune diseases, and conditions like COVID-19, symptoms may include fever, fatigue, and respiratory distress. If untreated, it can lead to serious complications or death. Management typically focuses on reducing inflammation and moderating the immune response.) The definitive laboratory diagnosis relies on the identification of viral ribonucleic acid (RNA) through real-time polymerase chain reaction (RT-PCR) testing of samples obtained from nasal and oropharyngeal swabs. This testing method is most effective when conducted in the initial days following symptom onset. Serological tests play a crucial role in assessing the immune response, as both IgM and IgG antibodies can be detected approximately seven days after the onset of symptoms and may persist for over 200 days. However, the presence of antibodies does not necessarily indicate that an individual is no longer infectious, as this depends on their viral load and clinical status. Utilizing specific laboratory markers judiciously is essential, considering the disease's progression. Proper interpretation of these markers can enhance patient management, facilitate the identification of asymptomatic carriers, and assist in monitoring those with mild symptoms.

Introduction and Definition :

Coronaviruses (CoVs) are enveloped viruses, measuring 60 to 120 nm in diameter, with a positive-sense, single-stranded RNA genome ranging from 26 to 32 kilobases. These viruses have pleomorphic capsids and crown-like surface projections, which is the origin of their name. The novel coronavirus, classified within the order Nidovirales and family Coronaviridae, was designated as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the International Committee on Taxonomy of Viruses. The World Health Organization (WHO) named the disease caused by this virus COVID-19 in February 2020.

Coronaviruses are categorized into three groups:

- α-CoVs
- β-CoVs
- γ-CoVs

They primarily infect birds and mammals, with α- and β-CoVs also capable of infecting humans. These infections typically target the upper respiratory tract, resembling common colds, but can lead to severe respiratory complications. Among the coronaviruses known to infect humans, two—SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV)—are associated with more severe outcomes, having caused notable outbreaks in China and the Middle East. Zoonotic transmission has been observed, with the novel coronavirus showing significant genetic similarity to coronaviruses found in Chinese horseshoe bats. This virus binds to the angiotensin-converting enzyme 2 (ACE2) receptor, facilitating its entry into human cells. In December 2019 and January 2020, atypical pneumonia cases (COVID-19) were reported in Wuhan, China. These cases, initially testing negative for SARS-CoV, were later found to be related to a new coronavirus, classified within the β-coronaviruses. The initial cases were linked to a seafood market in Wuhan, suggesting zoonotic transmission, followed by human-to-human transmission. Asymptomatic individuals can also spread the virus, emphasizing the need for hygiene and self-isolation. Transmission primarily occurs through respiratory droplets and contaminated surfaces. Studies indicate that viral particles can remain viable on various materials for hours to days, with effective disinfection methods significantly reducing viral loads. The incubation period for COVID-19 ranges from two to 14 days, with initial symptoms including fever, cough, and fatigue. Severe cases can lead to respiratory failure and increased mortality, particularly among the elderly and those with comorbidities.Following the identification of COVID-19, cases in China surged rapidly, prompting the WHO to declare it a pandemic in March 2020. As of May 1, 2020, over four million cases and more than 280,000 deaths were reported globally. In Brazil, the first confirmed case was noted on February 26, 2020, with significant spread leading to widespread community transmission.

Clinical Presentation of SARS-CoV-2 Infection :

SARS-CoV-2 infection can manifest in three main ways: asymptomatic carriers, acute respiratory disease (ARD), or varying degrees of pneumonia.

Initially, diagnosing asymptomatic carriers proved challenging due to differing testing protocols globally. Pediatric cases, often asymptomatic carriers, require particular attention to prevent transmission. Patients with positive molecular tests typically exhibit respiratory symptoms indicative of pneumonia, including fever, cough, myalgia, and fatigue, alongside other symptoms like respiratory secretions, headache, hemoptysis, and diarrhea.

Early symptoms may mimic those of other respiratory viruses like Noroviruses and Influenza. Dyspnea and high fever distinguish COVID-19 from a common cold, while similarities with Influenza exist, with COVID-19 having a higher tendency towards severe outcomes. Severe cases may progress to sepsis, marked by extrapulmonary involvement leading to heart and kidney damage, necessitating renal replacement therapy in about 20% of critically ill patients.

Screening tools like Sequential Organ Failure Assessment (SOFA) aid in early diagnosis and management, predicting patient outcomes. Anosmia/ageusia without nasal symptoms suggests potential direct neurological effects of SARS-CoV-2, requiring further research. Clinical data shows that most patients have a good prognosis, with a small percentage requiring oxygen therapy and intensive care, especially those with pre-existing conditions like diabetes, cardiovascular, and kidney diseases.

- Comorbidities such as diabetes, cardiovascular, and kidney diseases increase the risk of severe progression, including pneumonia and ARDS, often accompanied by cardiac, hepatic, and kidney dysfunction.

Laboratory Assessment in COVID-19: General and Specific Tests :

The clinical laboratory serves as a vital tool for diagnosing, monitoring, and understanding the progression and prognosis of both active and inactive pathologies. Amid the COVID-19 pandemic, various biomarkers have emerged as indicators of disease status and prognostic factors. Common laboratory findings in SARS-CoV-2 infection include leukocytosis or leukopenia, lymphopenia in the initial stages, and neutrophilia linked to poor prognosis.

Prominent alterations in COVID-19 patients comprise a 7%-80% rise in C-reactive protein (CRP), a 10%-88% reduction in serum albumin, and fluctuating total leukocyte counts, often showcasing lymphopenia. Hemoglobin levels drop by around 41%-70%, while markers like erythrocyte sedimentation rate (ESR), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) can vary between 8%-70%, and lactate dehydrogenase (LDH) levels increase by approximately 12%. As COVID-19 severity escalates, infection-related biomarkers like CRP, procalcitonin (PCT), and ESR gradually elevate. Additionally, D-dimer, creatine kinase (CK), creatine kinase-MB fraction (CK-MB), LDH, ALT, AST, urea, creatinine, cardiac troponin, and serum amyloid A protein surge. Notably, interleukin-6 (IL-6) levels rise with SARS progression, particularly in pneumonia and respiratory complications.

In critical care settings, patients exhibit heightened cytokine levels, lymphopenia, prolonged prothrombin time, and elevated LDH, D-dimer, PCR, and transaminases. Comparisons with SARS-CoV and MERS-CoV infections reveal similar laboratory anomalies. The platelet/lymphocyte ratio (PLR) and monocyte distribution width (MDW) serve as potential prognostic markers, reflecting disease severity and clinical outcomes.

Viral nucleic acid tests, especially RT-PCR, stand as the primary diagnostic method for COVID-19. Timely sample collection and proper handling are crucial for accurate results. RT-PCR's sensitivity and specificity make it indispensable, especially between days three and nine post-symptom onset. Immunological tests, while evolving, offer insights into antibody responses, aiding in diagnosis and monitoring disease progression.

In conclusion, laboratory diagnostics play a pivotal role in understanding and managing COVID-19, offering valuable insights into disease progression, severity, and treatment efficacy. Ongoing research aims to refine testing methods and enhance diagnostic accuracy in combating the pandemic effectively.

Key Insights on COVID-19 Laboratory Assessment :

The COVID-19 pandemic, caused by the novel coronavirus SARS-CoV-2, was declared a global health crisis by the WHO in 2020. This infectious disease poses significant risks to vulnerable populations, with a global fatality rate hovering around 6.8% as of early May 2020. Various factors such as age, immune status, social conditions, hygiene practices, and healthcare accessibility influence the mortality rates, with underdiagnosis and underreporting particularly prevalent in lower-income nations, potentially skewing mortality data.

Transmission primarily occurs through asymptomatic or mildly symptomatic individuals, contributing to the widespread dissemination of the virus. Severe cases of COVID-19 are associated with higher mortality rates compared to milder presentations. Clinical symptoms initially mimic those of Norovirus and Influenza, while severe cases manifest pulmonary complications akin to H1N1 influenza, SARS, and MERS-CoV infections.

Throughout the course of COVID-19 infection, several nonspecific laboratory parameters exhibit alterations, some of which hold prognostic value for monitoring disease progression. Laboratory analyses play a pivotal role in diagnosing COVID-19, tracking disease evolution, and predicting patient outcomes accurately. Moreover, these investigations underpin epidemiological studies that inform governmental healthcare strategies and evidence-based medical interventions.

The variability in RT-PCR positivity and seroconversion rates underscores the challenges in diagnosing asymptomatic cases accurately. Despite extensive research on COVID-19 pathophysiology, uncertainties persist regarding long-term immunity patterns in individuals with diverse clinical and laboratory profiles. Tailoring laboratory tests to different infection phases remains a critical area of investigation.

Epidemiological surveillance necessitates widespread collection of clinical samples for viral detection and immune response assessment to obtain a comprehensive understanding of the disease's global impact. Given the cost constraints associated with mass testing, judicious utilization of laboratory resources is imperative. Drawing insights from international literature, a practical framework has been developed to guide clinicians in the appropriate use of diagnostic markers for COVID-19 detection. Refer to Figure 3 for a detailed depiction of the applicability of laboratory biomarkers in COVID-19 assessment.

Summary of COVID-19 Clinical Features and Laboratory Diagnosis :

COVID-1P, caused by the severe acute respiratory syndrome coronavirus (SARS-CoV-2), emerged as a pandemic in 2002, recognized by the World Health Organization (WHO). This highly transmissible disease leads to severe outcomes in specific demographics, notably the elderly and individuals with immunodeficiencies, diabetes, cardiovascular conditions, or hypertension. Many infected individuals remain asymptomatic (potentially carriers) or exhibit mild to moderate flu-like symptoms. The most severe form of COVID-1P is characterized by a cytokine storm, hematological alterations, and coagulation changes that can culminate in tissue damage and mortality.

Nonspecific laboratory tests may exhibit varying levels depending on the disease progression and are often instrumental in predicting complications, such as through the assessment of D-dimer and the platelet-to-lymphocyte ratio. Specific laboratory diagnosis relies on real-time polymerase chain reaction (PCR) testing of nasal and oropharyngeal swab samples for viral ribonucleic acid (RNA), most effective within the early symptomatic phase. Serological tests play a crucial role in identifying immune responses, with IgM and IgG antibodies detectable from seven days post symptom onset, persisting for over 28 days. However, viral shedding and infectivity status remain independent of antibody presence, contingent on viral load and clinical presentation. Rational utilization of specific laboratory markers should align with disease progression timelines, aiding in patient management, and facilitating the identification of asymptomatic carriers or individuals with mild symptoms.

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