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Marcadores laboratoriais e achados de imagem da síndrome respiratória aguda grave causada pelo novo coronavírus (SARS-CoV-2): o que podemos encontrar?

Laboratory markers and image findings of a severe acute respiratory syndrome caused by the new coronavírus (SARS-CoV-2): what can we find?

Marcadores de laboratorio y hallazgos de imágenes del síndrome respiratorio agudo grave causado por el nuevo coronavirus (SARS-CoV-2): ¿qué podemos encontrar?

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Resumo

COVID-19 é uma doença infecciosa emergente que representa uma ameaça significativa à saúde pública mundial. Isso indica a necessidade de adesão a políticas pública a medidas preventivas, de controle e de diagnóstico rápido e preciso como parte das medidas de contenção ao avanço da pandemia. Este estudo se propôs analisar os principais achados laboratoriais da síndrome respiratória causada pelo novo coronavírus SARS-CoV-2 por meio de uma revisão narrativa da literatura. A técnica de detecção de RNA viral do coronavírus foi descrita como a principal metodologia utilizada para o diagnóstico clínico. Dentre os achados laboratoriais foi verificado a linfocitopenia, diminuição dos valores de hemoglobina e albumina sérica, aumento de lactato desidrogenase (LDH) e Proteína C Reativa (PCR), aumento da taxa de sedimentação de eritrócitos (VHS). O D-dímero foi relacionado a um mau prognóstico em pacientes críticos. No contexto atual, exames laboratoriais podem contribuir na identificação precoce de sinais de gravidade e mau prognostico da síndrome respiratória causada pelo novo SARS-CoV-2.

Palavras-chave: COVID-19; Marcadores laboratoriais; Achados de imagem; Síndrome respiratória.

Abstract

COVID-19 is an emerging infectious disease that represents a significant threat to public health worldwide. That indicates the need for adherence to public policies with preventive, control, and rapid and accurate diagnosis measures as part of the measures to contain the pandemic's advance. This study aimed to analyze the main laboratory findings of the respiratory syndrome caused by the new coronavirus SARS-CoV-2 through a narrative review of the literature. The coronavirus viral RNA detection technique has been described as the principal methodology used for clinical diagnosis. Among the laboratory findings, lymphocytopenia decreased hemoglobin and serum albumin values, increased lactate dehydrogenase (LDH) and C-reactive protein (CRP), increased erythrocyte sedimentation rate (ESR) were observed. D-dimer has been linked to poor prognosis in critically ill patients. In

the current context, laboratory tests can contribute to the early identification of signs of severity and poor prognosis of the respiratory syndrome caused by the new SARS-CoV-2.

Keywords: COVID-19; Laboratory markers; Image findings; Respiratory syndrome.

Resumen

COVID-19 es una enfermedad infecciosa emergente que representa una amenaza significativa para La salud pública en todo el mundo. Esto indica La necesidad de cumplir con las políticas públicas de medidas preventivas, de control y de diagnóstico rápido y preciso como parte de las medidas para contener el avance de la pandemia. Este estúdio tuvo como objetivo analizar los principal es hallazgos de laboratório del síndrome respiratorio causado por El nuevo coronavirus SARS- COV-2 por medio de una revisión narrativa de la literatura. La técnica para detectar ARN viral del coronavirus se describió como la metodología principal utilizada para el diagnóstico clínico. Entre los hallazgos de laboratorio, se verificaron los valores de linfocitopenia, disminución de hemoglobina y albúmina sérica, aumento de la lactato deshidrogenasa (LDH) y la proteína C reactiva (PCR), aumento de la velocidad de sedimentación globular (VSG). El dímero D se ha relacionado com un mal pronóstico en pacientes críticos. Em el contexto actual, lãs pruebas de laboratório pueden contribuir a la identificación temprana de signos de gravedad y mal pronóstico del síndrome respiratorio causado por el nuevo SARS-CoV-2.

Palabras clave: COVID-19; Marcadores de laboratório; Resultados de imagen; Síndrome respiratório.

1. Introduction

In China, at the end of 2019, a small group of patients with pneumonia of unknown cause was reported. Later, laboratory tests allowed the isolation and sequencing of a virus that crossed the barrier among species, initiating infection among humans. The new virus, belonging to the Coronavirus family, was named SARS-CoV-2, more popularly known as COVID-19 (Zhu, et al., 2020). Coronaviruses are enveloped positive RNA viruses (Huang, et al., 2020).

Since then, the virus has spread worldwide, infecting more than 11 million people and leaving a trail of death of approximately 500,000 people. The United States of America and Brazil release the ranking in the most number of cases, so far 2,911,888 and 1,603,055 cases have been reported respectively in these two countries (data from 07/06/20) (Johns Hopkins,

2020).

The virus is transmitted from one infected person to another, or by close contact, through contaminated objects and surfaces, secretions, coughing, sneezing, droplets of saliva, and handshake (Chan, et al., 2020). The mean interval between initial symptoms and death was 14 days (range 6 to 41 days) and was shorter (11.5 days) in patients aged ≥70 (Wang, et al., 2020).

Individuals at higher risk of severe illness included people over 60 years, mainly found in underlying conditions such as hypertension, diabetes, cardiovascular disease, chronic respiratory disease, and cancer. The clinical manifestations of COVID-19 appear after an incubation period of about 5 to 6 days and include more frequently fever, cough, and fatigue, with the possible onset of sputum production, headache, hemoptysis, diarrhea, dyspnea, among others (Guan, et al., 2020).

Also, complications occur in the lower respiratory tract, such as pneumonia and acute respiratory distress syndrome (SRAG), high fever, and headache. In most cases, the patient suffers from loss of taste and smell and severe gastrointestinal symptoms, as well as heart problems, the latter perhaps secondary to a cytokine storm (Huang, et al., 2020).

Although there are few studies regarding possible neurological manifestations of COVID-19, there is increasing evidence of neurological complications in affected patients, capable of generating long-term motor and functional deficits (Heneka, et al., 2020).

The definitive diagnosis of the new coronavirus is made with the collection of respiratory materials (airway aspiration or sputum induction). It is performed through the Polymerase Chain of the Real-Time (PCR-RT) technique and partial or total sequencing of the viral genome (Rodriguez-Morales, et al., 2020).

For the time being, no specific therapeutic agents and preventive vaccines are available and approved for COVID-19. However, many drugs used for other diseases have been tried in patients with SARS-CoV and MERS-CoV, and are undergoing an evaluation process in order to discover their effectiveness for the treatment of COVID-19. The drugs include remdesivir, baricitinib, chloroquine, hydroxychloroquine, the interleukin-6 receptor monoclonal antibody (IL-6) tocilizumab, and the anti-influenza drugs favipiravir and umifenovir (Cevik, et al., 2020).

For the prevention of the new coronavirus, health institutions recommend habits related to personal hygiene, such as washing hands with soap and water, frequently sanitizing personal objects, avoiding physical contact, among other recommendations (Chan, et al., 2020).

Presumptive diagnoses of infectious diseases are sometimes based on symptomatology and radiological examinations. However, the definitive diagnosis depends on the collection of the material and the correct identification of the infectious agent. In this context, laboratory tests provide relevant information, helping in the correct diagnosis. This study aimed to analyze the primary laboratory markers and findings of the respiratory syndrome caused by the new coronavirus SARS-CoV-2 through a narrative review of the literature.

2. Methodology

This research deals with a review of the scientific literature published so far, of a qualitative and descriptive nature, carried out from April to July 2020. The search occurred in the virtual health library databases, refined by the sources of Latin American and Caribbean Literature in Health Sciences (LILACS), and Scientific Electronic Library (SCIELO) and BIREME (Regional Library of Medicine), MEDLINE. Data were collected by simple random sampling, according to the scientific research elaboration manual proposed by Pereira et al (2018). The inclusion criteria adopted were: the availability of complete articles in Portuguese and English, published in 2020, in the databases mentioned above, and which addressed laboratory and imaging findings of the new COVID-19. The exclusion criteria recommended were published articles that did not address the proposed theme.

The descriptors used were: COVID-19, laboratory and imaging findings, and respiratory syndrome. The collection process of the material was performed in a non-random way from April to June 2020. Finally, these materials were read in full, categorized, and critically analyzed. In the initial research, approximately 2,000,000 publications addressing the new disease were found. Using the Boolean operator and, the search was reduced to 629 articles, of these 4 were experimental studies and two metanalysis addressing the laboratory markers of COVID-19. In addition, 122 studies were found addressing image findings, of which four were excluded by duplicates, and 123 because they did not meet the objective of the present study or were not available in full. The 21 selected works were analyzed in their entirety and were addressed in the tables and body of the text.

3. Literature Review and Discussion

The coronavirus RNA detection technique was the principal methodology used for clinical diagnosis. The latest serological tests were developed for IgM and IgG antibody

detection using techniques such as capillary immunochromatography assay and the enzyme-linked immunoassay (ELISA). The findings of the main studies are described in Table 1. Main typical and atypical imaging findings described in the literature for severe acute respiratory syndrome caused by the new SARS-CoV-2 are described in Table 2. Clinical significance of laboratory findings described in the literature for severe acute respiratory syndrome caused by the new SARS-CoV-2 is described in Table 3.

Table 1 - Main laboratory markers described in the literature for severe acute respiratory syndrome caused by the new SARS-CoV-2.

Laboratory findings	Huang, et al., 2020	Chen, et al., 2020	Chen, et al., 2020	Guan, et al., 2020
Lymphocytes	Decreased in 26 (63%) of 41 patients. Lymphocytes $<1.0\times10^9$ /L	Decreased by 9% of patients	Decreased by 69% of patients	Decreased. Average of $<1.0\times10^9$/L
Cytokines	High levels of IL2, IL7, IL10, GSCF, IP10, MCP1, MIP1A and TNFα	-	-	-
D-dimer	<2.4 mg/L in ICU patients	Increased in 36% of patients	-	High in 46% of cases
Transaminases	Increase of enzymes in 15 (37%) of 41 patients.	High AST in 35% of cases	High AST in 24% of cases	AST elevated in 22% of cases
Hemoglobin	-	Decreased by 51%	-	Normal
Albumin	-	Decreased by 98%	Decreased by 51%	-
LDH	Increased by 73%. Average 286.0 U/L (242.0-408.0)	Average 336.0 U/L (260.0-447.0)	Increased in 20 patients (68%)	Greater than ≥ 250 U/L in 41%of patients
C-Reative protein	-	High in 63 of the cases (63%)	Elevated in 27 out of 29 patients	High in 481 of the 793 cases

Source: elaborated by the authors.

Table 2 - Main typical and atypical imaging findings described in the literature for severe acute respiratory syndrome caused by the new SARS-CoV-2.

Moreira, et al., 2020	Poorly defined lung opacities, frosted glass opacities
Muniz, et al., 2020	Multifocal areas of opacities in frosted glass, with small areas of consolidation, subpleural and peripheral involvement in the lingula.
Moreira, et at., 2020	Peripheral opacities of frosted glass, development of consolidation, laminar pleural effusion, cardiomegaly, acute embolism, pulmonary infarction.
Farias, et al., 2020	Frosted glass opacities associated with some prominent lower lobe (CT) consolidations. Slight thickening of the inter and intralobular septa that constitute the pattern at the base of the lung.
Carvalho, et al., 2020	Airway space compromise, pleural effusion, severe colon inflammation, hemorrhagic colitis.
Ramaswamy & Govindarajan, 2020	Infiltrates irregularly in the lower lobes.
Chate, et al., 2020	Peripheral frosted glass opacities, interlobular septum thickening, bilateral consolidations, pleural effusion.
Rosa, et al., 2020	Frosted glass opacity, mosaic paving, pleural effusion, consolidation.
Zhang, et al., 2020	Ventricular dilation, impaired function (transthoracic echocardiography)
Craver, et al. 2020	Eosinophilic myocarditis
Novara, et al., 2020	Severe acute gangrene
Novi, et al., 2020	Acute disseminated encephalomyelitis
Ucpinar, et al., 2020	Pneumothorax and subcutaneous emphysema

Source: Elaborated by the authors.

Table 3 - Clinical significance of laboratory findings described in the literature for severe acute respiratory syndrome caused by the new SARS-CoV-2.

Lymphocytopenia	Decreased immune response to infectious agents, especially viral
Increase of cytokines	Inflammatory response exacerbated
D-Dimer Augmentation	Its increase has been attributed to complications and poor prognosis of the respiratory syndrome and increased thrombotic events.
Increase of Transaminases	Liver injury or widespread organ damage
Hemoglobin Decrease	Functional reduction of RBCs and impairment of O2, accentuation of dyspnea
Albumin Decrease	Liver function commitment
LDH Increase	Associated with lung injury and widespread organ damage
Reactive C Protein Increase	Inflammatory process underway.

Source: Elaborated by the authors.

In the Table 1 it is possible to notice that the main markers identified as altered were: the lymphocotypenia described in the 4 articles that carry out experimental analyzes in patients confirmed with COVID-19; Huang found a significant increase in inflammatory proteins, mainly cytokines, LDH and C-reactive protein. The D-dimer was increased in all studies analyzed, and it was shown to be higher in critically ill patients with poor prognosis. Alterations in liver enzymes and albumin demonstrate important hepatic impairment during acute respiratory syndrome.

In the Table 2, we note that most authors reported the occurrence of ground-glass opacities, isolated or multifocal, also the presence of consolidations, aerobocograms, decreased air spaces, cardiomegaly and pleural effusion as the common findings of the syndrome. Among the atypical findings, myocarditis, gangrene, encephalomyelitis and the presence of pneumothorax and emphysema were found.

In this Table 3, the clinical significance of the laboratory markers described as altered by the literature can be found. lymphocytopenia, decreased hemoglobin and increased levels

of D-dimer indicate a poor prognosis of the disease, resulting in increased dyspnea and a higher occurrence of thrombotic events such as disseminated intravascular coagulation; increased transaminase and decreased albumin were associated with hepatic impairment in patients with COVID-19.

Initial investigations also included a complete blood count, coagulation profile, serum biochemistry tests such as renal and liver function, creatine kinase (CK), lactate dehydrogenase (LDH), and electrolytes. Among the findings were lymphocytopenia, decreased hemoglobin, and serum albumin values, increased lactate dehydrogenase (LDH), and C-reactive protein (PCR), increased erythrocyte sedimentation rate (VHS) (Huang, et al., 2020).

The known radiological characteristics of COVID-19 pneumonia at CT are extensive bilateral opacification in frosted glass, involving mainly the lower lobes and consolidations, reduction of air spaces, pleural effusion, vascular thickening. Chest radiological examination revealed that most patients with coronavirus pneumonia presented bilateral lung injury (72.9%), characterized mainly by frosted glass opacities (68.5%).

Unusual characteristics were found, such as pleural and pericardial effusion, lymphadenopathy, cavitation, pneumothorax, emphysema, encephalomyelitis, gangrene, hemorrhagic colitis, myocarditis, and myasthenia gravis. During the acute phase of infection with COVID-19, about 36% of the cases evaluated in one study developed neurological symptoms, 25% of which can be attributed to the direct involvement of the central nervous system.

So far, it has been inferred that coronavirus infections may be associated with myopathies. In recently published studies on COVID-19 in China, myalgia or fatigue affected 44% to 70% of hospitalized patients, and increased creatine kinase (CK) was present in up to 33% of admitted patients. No additional tests, such as EMG, muscle imaging, or histopathology, were reported (Guindon, et al., 2020).

RT-PCR (*reverse-transcriptase polymerase chain reaction*) is considered the gold standard in COVID-19 diagnosis. Confirmation is obtained through the detection of SARS-CoV-2 RNA in the analyzed sample, preferably obtained from nasopharynx scrape. Molecular techniques have been successfully used to identify infectious agents for many years. Sequencing, although a high-cost technique, has been a powerful tool for describing the pathogen in the work of Zhu, et al (2020).

SARS-CoV-2 RNA was identified by qRT-PCR in respiratory tract samples 1 to 2 days before the onset of symptoms and may remain for 7 to 12 days in moderate cases and up

to 14 days in severe cases. Asymptomatic cases were also confirmed at the time of laboratory testing. Transmission is conventional by both asymptomatic and pre- asymptomatic people, becoming a challenge for contact tracing (Cevik, et al., 2020).

The concern with RT-PCR in real-time is the risk of obtaining false-negative and false-positive results. False-negative results may be related to mutations in the target regions of the primer and probe in the SARS-CoV-2 genome. The occurrence of a false positive in one or more of the reactions is indicative of sample contamination (Tahamtan & Ardebili, 2020).

Serology, unlike RT-PCR, checks the body's immune response to the virus. Tests using the serology methodology evaluate the amount of IgM and IgG type antibodies that the immune system produces when it comes into contact with an antigen. In the case of SARS-CoV, the serology test is positive 7 to 11 days after contact with the virus. In Brazil, there are currently 17 approved tests, nine of which are chromatographic immunoassay tests for the detection and differentiation of IgM and IgG antibodies. The samples tested are usually whole blood, serum, or plasma.

The tests have a membrane system in which human IgG and anti-IgM antibodies are immobilized in the IgG test region and the IgM test region. The specificity for IgM class antibodies ranged from 94% to 98%, and IgG from 97% to 98% according to the manufacturer and sensitivity for IgM type antibodies ranged from 85% to 90% and for IgG type antibodies from 95% to 100% (Brazilian Ministry of Health, 2020).

Traugott et al. (2020) demonstrated in a study that the sensitivities of the evaluated anti-SARS-CoV-2 IgM and IgA ELISA were low within five days after the onset of the disease, but subsequently increased to 84% IgA and 92% for IgM between 6 and 10 days after the onset of symptoms.

However, most of the existing rapid tests have very low sensitivity and specificity compared to other methodologies. The Brazilian Ministry of Health (2020) points out that rapid tests have an error rate of 75% for negative results, which can generate uncertainty and uncertainty to interpret a negative result and determine whether or not the patient in question needs to maintain social isolation. Antibody test results should not be used as the sole basis for diagnosing or ruling out SARS-CoV-2 infection or for reporting the infection status (Matushek, et al., 2020).

Additional evidence to confirm infection includes identification of a 2019-nCoV antigen in patients' lung tissue by immunohistochemical analysis, detection of IgM and IgG antiviral antibodies in patients' serum samples (Zhu, et al., 2020).

In the meta-analysis of Rodrigues-Morales et al. (2020), several studies were gathered describing the following laboratory findings: decreased albumin (75.8%), increased C-reactive protein (58.3%), increased lactate dehydrogenase (LDH) (57.0%), decreased lymphocytes (43.1%) and increased erythrocyte sedimentation rate (VHS) (41.8%). Also, the chest radiological examination revealed that most new patients with coronavirus pneumonia presented bilateral lung injury (72.9%), characterized mainly by frosted glass opacities (68.5%) (Rodriguez-Morales, et al., 2020).

In studies published on COVID-19 in China, myalgia or fatigue affected 44% to 70% of hospitalized patients, and increased creatine kinase (CK) was present in up to 33% of admitted patients. No additional tests, such as EMG, muscle imaging, or histopathology, were reported (Guidon, et al., 2020).

One of the laboratory findings found in the new SARS-COV-2 coronavirus infection is lymphopenia present in over 40% of patients. This may occur due to the immune response caused by SARS-CoV-2, which is cell-mediated. According to the study by Dhama et al. (2020), SARS-CoV-2 stimulates an immune response mediated by T and B lymphocytes. The virus initially attacks the cells of the epithelium of the respiratory mucosa and from there spreads and infects other cells, especially the T lymphocytes. This causes a storm of inflammation in the body generating immune responses that alter peripheral leukocytes such as lymphocytes. The damage caused to these cells by the coronavirus leads to the development of lymphopenia that predisposes to secondary infections and increases the severity of the case. In the metanalysis of Lippi & Mattiuzzi (2020), it was shown that hemoglobin levels are reduced mainly in patients considered severe.

SARS-CoV-2 interacts with the hemoglobin molecule through receptors such as ACE2, CD147, CD26 located in red blood cells and blood precursors. The virus is believed to attack the heme portion of the 1-beta hemoglobin chain leading to hemolysis and formation of a complex with the free heme portion, thus generating abnormal hemoglobin that has compromised the transport of O2 and CO2. These findings are responsible for a significant reduction in functional hemoglobin, especially in the more advanced stages of SARS-CoV-2 infection (Cavezzi, et al., 2020).

Furthermore, it suggested that the CD147 and CD26 receptors attack the erythroblasts of the bone marrow because due to the larger size and material of the cytoplasm and nucleus of these cells, viral replication and interaction with the hemoglobin molecule is favored. The gradual reduction of hemoglobin may lead tosideroblastic pattern anemia, with myelodysplastic characteristics, according to the need for replacement of dysfunctional

erythrocytes (Cavezzi, et al., 2020).

D-dimer (or dimer D) is the residual products of fibrin degradation (PDFs) present in the blood after the degradation of a blood clot by fibrinolysis. They are usually not present in human blood plasma except when the clotting system has been activated, for example, due to the presence of thrombosis or disseminated intravascular coagulation. False-positives can be caused by several causes: liver disease, high rheumatoid factor, inflammation, tumors, trauma, pregnancy, recent surgery, and advanced age (Tahamtan, & Ardebili, 2020). Currently, this marker has been highlighted for being used in the diagnosis of disseminated blood disorder by intravascular coagulation in the COVID-19. A four-fold increase in protein is a reliable indicator of mortality in those suffering from this disease.

In the study by Huang et al. (2020), this marker was increased among patients with COVID-19 are admitted to the ICU compared to patients who did not go to the ICU [$p = 0.0042$]. This marker has been attributed to complications and poor prognosis of a respiratory syndrome caused by SARS-CoV-2. In the study of Xu et al (2020), 65.3% of the 72 patients with the disease presented thrombotic events.

The D-dimer level of patients with the disease gradually increased with the worsening of the disease. The authors concluded that the D-dimer levels in patients with COVID-19 are correlated with inflammatory factors and organ function and can be used to predict severe organic injuries [$p<0.05$]. Another study reported that the association of IL-6 and D-dimer results had a sensitivity of 96.4% and specificity of 93.3% to predict early the severity of COVID-19 in adult patients (Gao, et al., 2020).

Aminotransferases (alanine aminotransferase - TGP and aspartate aminotransferase - TGO) are enzymes present within the liver cells, and therefore their alteration is directly linked with dysfunctions in this organ. With the death of these cells, by liver disease or other reasons, these enzymes come out of the cells and end up in the blood, appearing increased in the laboratory examination. They are therefore measured to indicate leakage of cells damaged by inflammation or cell death (ABCMED, 2016). The reference values of liver markers (Aspartate aminotransferase (AST/TGO) for men up to 40 U/L, women up to 32 U/L; alanine aminotransferase (ALT/TGP) for men up to 41 U/L, women up to 33 U/L (Bahia, et al., 2014).

Data from the Fifth PLS General Hospital Medical Center, Beijing, China, indicate that 2-11% of patients with COVID-19 had liver comorbidities. Furthermore, from 14 to 53% of the cases reported abnormal levels of the hepatic enzymes alanine aminotransferase and aspartate aminotransferase (AST) during the progression of the disease, indicating that the

damage caused by the virus is not restricted to those who had pre-existing liver diseases. The highest rates of liver dysfunction occurred among patients with severe COVID-19. In another published study, AST elevations were observed in eight (62%) of 13 patients in a Chinese intensive care unit (ICU) compared to seven (25%) of 28 patients who did not need ICU care (Huang, et al. 2020).

Even not being used as routine screening, imaging exams such as computed tomography (CT) and Nuclear Magnetic Resonance (NMR) are strongly recommended for suspected cases of COVID-19, especially in severe cases, both in the initial assessment and follow-up. The known radiological characteristics of COVID-19 pneumonia at CT are extensive bilateral opacification in frosted glass, involving mainly the lower lobes and consolidations, reduction of air spaces (Moreira, et al., 2020; Muniz, et al., 2020; Farias, et al., 2020, Chate, et al., 2020).

Unusual characteristics were found, such as pleural and pericardial effusion, lymphadenopathy, cavitation, pneumothorax, emphysema, encephalomyelitis, gangrene, hemorrhagic colitis, myocarditis, myasthenia gravis (Ucpinar, et al. , 2020; Novi, et al., 2020, Novari, et al., 2020; Carvalho, et al. 2020, Craver, et al., 2020; Ramaswamy & Govindarajan, 2020).

Although the neurological manifestations of COVID-19 have not been adequately studied, there is growing evidence that reports infection caused by Sars-CoV-2 and its ability to generate neurological deficits. In the literature at the moment, it is known that patients in severe cases of COVID-19 presented high levels of pro-inflammatory cytokines and respiratory dysfunction, factors of which suggest a cognitive decline. Pathogenically, this can generate direct adverse effects of immune reaction, worsening of pre-existing cognitive deficits, or induction of a new neurodegenerative disease (Heneka, et al., 2020).

During the acute phase of COVID-19 infection, about 36% of the cases evaluated in one study developed neurological symptoms, 25% of which can be attributed to the direct involvement of the central nervous system. There were neuropathological findings in the autopsy of a patient who died due to complications caused by COVID-19. Hemorrhagic lesions of the white matter were present in the cerebral hemispheres with surrounding axonal lesions and macrophages. The subcortical white matter had scattered groups of macrophages, a variety of associated axonal lesions, and an appearance similar to perivascular acute disseminated encephalomyelitis (Needham, et al., 2020).

The presence of the virus often generates morphological changes in the host cell, and any change in the host cell due to infection is known as the cytopathic effect. They consist of

cell curvature, disorientation, swelling or withering, death, surface detachment, among other changes. According to Margaret Hunt (2020), many viruses induce apoptosis in infected cells, either due to the pathogenicity mechanisms used by invaders or the host damage limitation response. In the work of Zhu, et al. (2020), this effect was demonstrated in the laboratory by the new coronavirus. They also visualized abundant intracellular inclusions in transmission electron microscopy (MET).

These datas suggest that COVID-19 is an emerging infectious disease that poses a significant threat to global public health. This indicates the need for public policy adherence to preventive, control, and rapid and accurate diagnostic measures as part of the measures to contain the advance of the pandemic. Therefore, early diagnosis and timely treatment of critical cases are extremely crucial. Currently, the occurrence, development, prognostic mechanism, and immune status of patients with COVID-19 are still not entirely clear.

4. Conclusion and Suggestions

Managed care of patients with SARS-CoV-2 infection involves early identification, rapid isolation, the timely establishment of infection prevention and control measures (CPI), along with symptomatic care for patients with mild disease and supportive treatment for those with severe COVID-19. In this context, laboratory and imaging tests can contribute to the early identification of signs of severity and poor prognosis of the respiratory syndrome caused by the new SARS-CoV-2.

We suggest the training of health professionals to early identify the signs and symptoms characteristic of the new coronavirus, training of professionals in the collection of samples for correct collection, transport and storage of samples in a timely manner. Investment in laboratory infrastructure, such as the acquisition of automated systems for the processing of high-performance samples, for simultaneous processing of numerous samples, which will allow, in addition to the precision of results, a rapid analysis that will contribute to early decision-making and comprehensive assistance to affected patients. by the new COVID-19. We also recommend that the radiological diagnostic tools are not underestimated, although they are not indicated for diagnostic confirmation, they can offer important clinical information about the disease.

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