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TÍTULO: La carga viral y los biomarcadores químicos para evaluar la gravedad y el pronóstico en pacientes con SARS-CoV-2.

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RESUMEN: Este trabajo es una revisiónbibliográfica de artículoscientíficos de alto impacto que se han publicado en los últimos meses sobre el SARS-CoV-2. Se ha reportado que el COVID-19 tiene una alta transmisibilidad y mortalidad, y por ser un virus emergente se han realizado investigaciones sobre sus mecanismos de virulencia y patología; por esta razón, en este estudio se detalla minuciosamente las características moleculares, fisiopatología y la respuesta inmunitaria del paciente frente a la infección, ya que puede ser exacerbada y causar falla multiorgánica desatando el aumento de biomarcadores inflamatorios y de coagulación, que tienen que ser interpretados por el tratante debido a que el aumento exponencial de ferritina, D-Dimero, LDH, Procalcitonina (PCT), se correlacionan como de mal pronóstico del paciente.

PALABRAS CLAVES: SARS-Cov-2, Biomarcadores, Carga Viral, Laboratory, Pronóstico COVID-19.

TITLE: The viral load and chemical biomarkers to evaluate the severity and prognosis in patients with SARS-CoV-2.

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ABSTRACT: This work is a bibliographic review of high impact scientific articles that have been published in previous months on SARS-CoV-2. It has been reported that the COVID-19 has a high transmissibility and mortality;as it an emerging virus, research has been carried out on its mechanisms of virulence and pathology; for this reason,in this study, the molecular characteristics, pathophysiology and the immune response of the patient against infection are detailed since it can be exasperating and cause multiorgan failure, unleashing the increase in inflammatory and coagulation biomarkers, which have to be interpreted by the treating physician because the exponential increase in ferritin, D-Dimer, LDH, Procalcitonin (PCT), is correlated as a poor prognosis of the patient.

KEY WORDS: SARS-Cov-2, Biomarkers, Viral load, Laboratory, COVID-19 prognosis.

INTRODUCTION.

The WHO reported some cases of unknown pneumonia in the province of Wuhan – China on December 31st, 2019, working tirelessly to identify the threatening virus;finally, the complete genotype of the virus was possible to sequence on January 12th. It was defined as 2019-nCov, a virus of the coronaviridae family, order Nidoviridae that causes severe acute respiratory syndrome(Huang et al. 2020), the product of a zoonotic disease by the consume of bats and pangolin (Zhang, Wu, y Zhang 2020), it has caused great concern due to on January 30th were

confirmed 6000 cases with 132 deaths on most continents with the exception of Latin America, the WHO declared a public health emergency of international importance (WHO , 2020).

On March 11th was declared a pandemic with 118 319 cases and 4292 confirmed deaths worldwide (WHO , 2020); the pressure and concern of health staff are strong for not containing the infection, the SARS-CoV-2 causes an unfavorable prognosis in people with pre-existing comorbidities (Wang et al. 2020); the risk of mortality rises in adults older than 60 years, who have diabetes, obesity, cardiovascular disease and high blood pressure (Wu et al. 2020a), since the viral replication causes an intense immune response increasing the cellular and adaptive response producing a macrophage logic activation syndrome with a "cytokine storm syndrome¨ and inflammasome and an immunotrombotic response characterized by thrombocytopenia and in critical cases intravascular coagulopathy with exacerbated increase of inflammatory markers causing alveolar damage (Ulhaq y Soraya 2020)(Cao 2020). Bacterial sepsis should be added in patients who are in the Intensive Care Unit (Lippi y Plebani 2020).

The laboratory plays an important role in early detection of SARS-CoV-2 thanks to quantitative markers that help control the patient's prognosis, inflammatory indicators such as interleukin VI, Ferritin, D-dimer (Huang et al. 2020); as well as the viral load that plays a very important role in assessing the severity of the disease and monitoring the innate and adaptive immune response that seems to have an inverse relationship with antibodies detected in the serum of the patients (To et al. 2020a).

The main objective of this article is to correlate the viral load of the patient infected with SARS-CoV-2 with clinical biomarkers, as well as the pathophysiology of infection and alteration of clinical markers, establishing the markers of poor prognosis in hospitalized.

For thisresearch, a meta-analysis was performed (Moher et al. 2009) and electronic search in PubMed, Scopus, and Web of Science, using keywords such as ¨SARS –CoV-2¨,

¨Biomarkers¨,¨Viral load¨. ¨Laboratory, COVID-19 prognosis¨. The articles cited were examined by researchers and undergraduate students from the Regional Autonomous University of the Andes. Our study will help health care staff to treat and assess the health status of patients diagnosed with SARS-CoV-2.

DEVELOPMENT.

Materials and methods.

A systematic review of scientific articles was carried out with a meta-analysis and data collection, from which were chosen those that explained the physiopathology and viral load presented by hospitalized patients with SARS-CoV-2, the laboratory data was correlated with the clinic of the patients.

The scientific opinion articles were debugged because they did not have relevant information on the subject.

Information sources and search strategy.

An exhaustive review was carried out in bibliographic search engines such as Scopus, Web of Science, PubMed, as well as in high impact journals such as The Lancet Infection Diseases, Nature Reserch, Science research Journal, searching for keywords like: ¨SARS-CoV-2¨, ¨Biomarkers¨, ¨Viral load¨, ¨Laboratory, COVID-19 prognosis¨, the search started on April 30th, 2020.

The articles were selected according to the title and the abstract, the laboratory results with the inflammatory and coagulation markers were included, a qualitative synthesis of the results was made and the viral load of the patients was correlated with the increase of the biochemical levels; considering as a priority, patients admitted to the ICU, with comorbidities such as obesity, diabetes mellitus type II, arterial hypertension, older adults and patients admitted with ARDS (Acute Respiratory Distress Syndrome).

Results.

Molecular diagnosis and viral load.

Previous studies show that the RaTG13 genome of SARS-CoV-2 has 103 mutations in bats with a possible recombination in pangolin, so it has been shown two strains, named as L and S. The S-train is originated in Wuhan while the L-strain had evolved, and it is the most detected (Tang et al. 2020).

In April, more than 51 protein mutations have been determined in the ORF3a genes that give it virulence and infectivity since they are in charge of interacting with NF-KB and inflammasome (Issa et al. 2020). In May, the genotype and phenotype of COVID-19 involved, it´s virulence mechanism had a mutation with greater infectivity and transmissibility. This alteration occurred at 11,083 position of Nsp6 gene in Orfl, altering the expression of the adaptative cellular response of lymphocytes CD4 cytotoxic (Van Dorp et al. 2020).

The viral load of the infected patients was determined using the reverse transcriptase quantitative PCR (RT-qPCR) technique. The patients were previously treated with Nasopharyngeal and throat swabs, the concentration of the virus was quantified and reached 104 and 108 genomic copies / ml. The viral load could be determined from the first day of the symptoms (Sethuraman, Jeremiah, y Ryo 2020). Although Fengting Yu mentions in his research that sputum is the best indicator to determine the patient´s viral load and the virus has a higher replication (Yu et al. 2020), the infected patients presented mild symptomatology after 5 and 6 days, with a gradually decreasing viral load, while severe patients had high transmissibility with a high viral load that was intense and very long lasting (To et al. 2020a).

The sensitivity of this molecular method correlates with the patient's prognosis and the infective dose. It can also detect up to 20 days and extends up to 37 days in patients who have overcome the disease (To et al. 2020a). There are patients who remained asymptomatic with a high viral load and

even patients with severe clinical conditions who have viral loads greater than 60 times in patients with mild conditions.

The COVID-19 has an incubation period of approximately 5 days, and patients develop symptoms 14 days later (Lauer et al. 2020).Determining viral load is especially important because it allows the doctor to give guidance on antiviral treatment. It was shown that a high viral load at the onset of the disease is inversely related to the serum antibody response and a poor prognosis. It was recognized that IgG concentration may increase at the same time or even before IgM immunoglobulins (To et al. 2020a).

The combination of important markers such as immunoglobulin IgM, C-reactive protein (CRP), qRT - PCR provide clinically relevant information on patient's severity (Yue et al. 2018) (Sethuraman et al. 2020). The IgM is an early specific marker of infectious disease, patients with severe pneumonia have an extremely high viral load, while IgG remain stable for months after contracting the infection (Shi et al. 2020).

Pathophysiology SARS – CoV-2.

The COVID-19 has the ability to recognize the angiotensin-converting enzyme 2 (ACE2) receptors, use its S-spike protein and adhere to the cell membrane of myocytes and vascular endothelial cells (Zhou et al. 2020a), using as a priming to the protein (TMPRSS2) cellular serine protease for S gycoprotein to enter the host (Hoffmann et al. 2020).

Viral replication is immediate causing rapid gene expression of the cellular response with macrophage activation and inflammatory markers such as chemokines, interleukins and IFN - γ (Zhou et al. 2020a), which cause apoptosis of pulmonary epithelial and endothelial cells, increasing vascular permeability and allowing extracellular fluid to enter the lung causing respiratory distress (Yilla et al. 2005).

The SARS-CoV-2 genome encodes eight proteins with open reading fragment (ORF) that increase the expression of cytokines and chemokines expressing a severe inflammatory phenotype important for pathogenesis producing programmed necrosis independent of caspases mediated by Rip1-Rip3-MLKLs that form pores causing cellular apoptosis and activation of the inflammasome that releases the molecular patterns associated with inflammatory damage (Yue et al. 2018).

In critical patients, in addition to the inflammatory response, the coagulation processes are activated, generating thrombin that obstructs the blood vessels, causing a disseminated intravascular coagulopathy (DIC), platelet and fibrin circulate until produce vascular injury inducing ischemia and thrombosis (Connors y Levy 2020). The thrombosis is associated with interstitial alveolar inflammation with macrophage activation and fibrinolysis with subsequent liver dysfunction exacerbates the consumptive coagulopathy, while in the pulmonary infiltration observed in computerized tomography diffuse alveolar changes are shown, ischemia product of coagulation factors that generate thrombosis myocarditis and cardiomegaly (McGonagle et al. 2020).

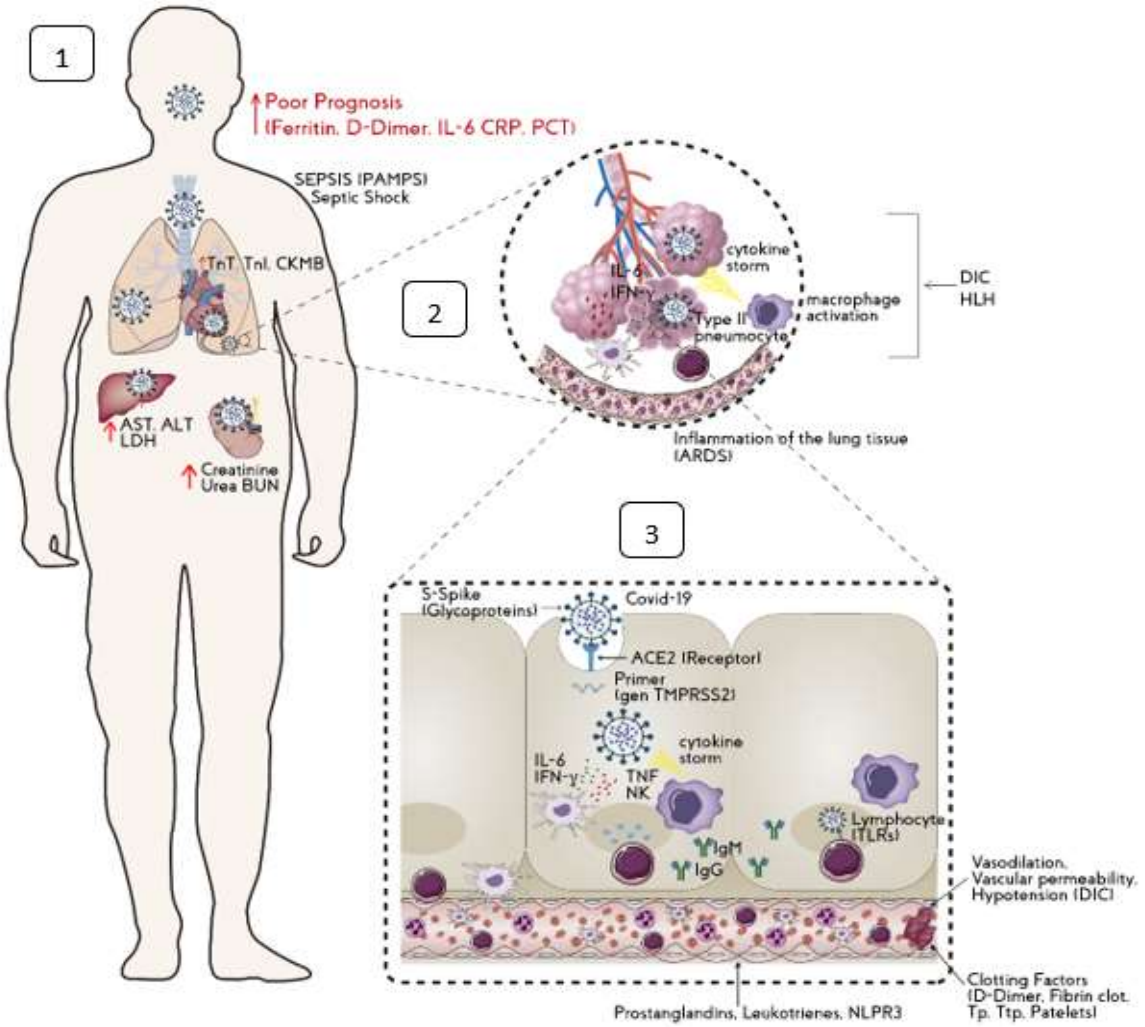

Figure 1: Pathophysiology of SARS-CoV-2: **Image 1**, patient with comorbidities (Type II Diabetes Mellitus, obesity, high blood pressure) with a high viral load and sepsis. **Image 2**, Macrophage activation with cytokine storm and proinflammatory markers such as IFN-γ, IL-6, TNF, that cause uncontrolled inflammation and injury to the lung tissue. **Image 3**Interaction of the COVID-19 S-spike with the ACE2 receptors of transmembrane proteins from myocytes and vascular endothelial cell, with the activation of the innate and adaptative immune response. IL-6: Interleukin, PAMPS: molecular patterns associated with pathogens, TnT-I: cardiac troponins, CK-MB: creatine kinase, AST-ALT: liver transaminases, LDH: lactate dehydrogenase, BUN: blood urea nitrogen, IFN- γ: Interferon, DIC: disseminated intravascular coagulopathy, SHLH: secondary hemophagocytic

lymphohistiocytosis, TLRs: Toll like receptors, Tp: trombin, Ttp: tromboplastin, IgG-IgM: inmunoglobulins. The figure was modified by the following authors (Li et al. 2020), (Tay et al. 2020)**,** (Akhmerov y Marban 2020)**.**

Immune response.

The severity of the patient is specifically correlated with the uncontrolled immune response by activation of the innate and adaptive response. When Covid-19 enters through endocytosis into the pulmonary alveoli, the innate response is activated which triggers the rise of interferon expressing genes for the antiviral response, along with dendritic cells that activate tumor necrosis factor (TNF) and IFN- α, these molecules spread through the vascular system and activate the coagulation processes (Zheng et al. 2020).

Subsequently, the adaptive response represented by B and T lymphocytes generate antibodies and secretecytotoxic IFN-γ which activates the inflammatory process, macrophages trigger a cellular response causing inflammasome, NLRP3 that produce a storm of cytokine, interleukin and chemokine that help to signaling. The toll like receptor (TLR) activates the nucleator factor (NF- kB) response generating injury and necrosis in tissues (Liu et al. 2020).

While patients with a high value of cytotoxic T-Lymphocytes and INF-γ, induce the expression of aberrant genes in lung endothelial cells activating the inflammatory signaling with cytokine rain and lung damage (Chen, Huarong et al. 2020).

Coagulation markers and SARS-CoV-2.

Important markers increase such as D-Dimer, Erythtocyte Sedimentation Rate (ESR), C-reactive protein (CRP), IL-6 interleukin, thrombin, thromboplastin, and platelets. Procoagulant and inflammatory changes are closely related since it has been determined that patients with high levels of IL-6 interleukin have increased fibrinogen (Ranucci et al. 2020).

In the early phase, there are coagulation abnormalities as well as increase of ESR, CRP, progressive lymphopenia, after 6 days of hospitalization increases the D-Dimer and coagulation factors TP and TTp, IL-6 but if thrombosis and ischemia occur, cardiac markers such as troponins increase and the patient may present arterial hypertension, generating chronic heart failure(Connors y Levy 2020).

The patients who develop ¨DIC¨ within 10 days of being hospitalized have an increase in the D-Dimer with decreased in fibrinogen and platelets generating tromboinflammation which in most cases is induced by bacterial sepsis. The coagulopathy may be confirmed with three indicators: elevated thrombin times, thromboplastin, and hypoproteinemia with decreased markers such as albumin, leukocytes, and lymphocytes (Connors y Levy 2020).

COVID - 19 and Sepsis.

When the patient presents a sepsis due to a bacterial over-infection, the inflammatory and coagulation factors are raised because the microorganisms have polyphosphates and PAMPs (pathogen-associated molecular patterns) in its external structure that interact with mast cells amplifying the immune response and increasing the Procalcitonin (PCT) marker (Connors y Levy.2020).It has been reported the death of patients by multiorgan failure, there is a cardiac, renal respiratory injury, in addition to a systemic inflammation of the lungs, multiorgan dysfunction, acute respiratory distress syndrome, and heart failure caused by mononuclear inflammatory infiltrates (Zhou et al. 2020a).

SARS-CoV-2 recovery patients.

Most of the recovered patients, who were not admitted to the ICU, were on average age of 50 years and female, who were hospitalized for two weeks and discharged when they presented low antibodies titers to SARS-COV-2 in their serum, with a low viral load of the E-wrap gene,

Nucleocapside N-gene, and RdRp gene. It is presumed that the controlled immune response and recovery is due to genetic factors attributed to the X chromosome (Chen, Nanshan et al. 2020b)and a low concentration of the ACE2 receptor in their cells (Wu, Fan et al. 2020) (Sethuraman et al. 2020). It has been shown that patients with interstitial pneumonia and lymphopenia have recovered without the need for mechanical assisted ventilation, thanks to a high cellular response of cytotoxic T-lymphocytes that express activation markers such as HLA-DR and CD38.

TABLE # 1. Compilation of laboratory results from 10 scientific articles: Blood count, blood proteins, inflammation markers and coagulation with your reference data. ¨CRP¨ stands for C-reactive protein, ¨LDH¨ lactate deshydrogenase, ¨IL-6¨ interleukin 6. N/R not (clearly) reported.

laboratoryresults	**(Yang et al. 2020)**	**(Henry et al. 2020) (Lippi y Plebani 2020)**	**(N. Chen et al. 2020b) (Han et al. 2020)**	**(Zhang et al. 2020)(N. Chen et al. 2020b)**	**(T. Chen et al. 2020a)**	**(C. Wu et al. 2020a)**	**(Zhou et al. 2020a)**	**Normal Values**
Leukocytes	7,25x10^9/L	4,1x10^9/L	0,079 x10^9/L	4,7 x10^9/L	6,2x10^9/L	5.94x10^9/L	6.2x10^9/L	4.5 - 11.0 × 109/L
Neutrophils	↑9,3×109/L	4,1x10^9/L	↓1,43 x10^9/L	↓1,06x10^9/L	5x10^9/L	4.47x10^9/L	N/R	2,5-7,5× **10^9/L,**
Lymphocytes	↑21,74× 109/L	0,28× 109/L	↑0,87 x10^9/L	16,9 x10^9/L	↓0.9 x10^9/L	↓0.9 x10^9/L	7.5x10^9/L	150 a 400 × 109/L
Platelets	259,54×10 9/L	↓23.36×10 9/L	214x10^9/L	261,5 x10^9/L	213.5x10^9 /L	180x10^9/L	206x10^9/L	100-300(*10^9 L-1)
Bloodproteins	(Yang et al. 2020)	(Henry et al. 2020) (Lippi y Plebani 2020)	(N. Chen et al. 2020b) (Han et al. 2020)	(Zhang et al. 2020)(N. Chen et al. 2020b)	(T. Chen et al. 2020a)	(C. Wu et al. 2020a)	(Zhou et al. 2020a)	**Normal Values**
CRP	↑34,33mg/l	↑37.78mg/l	6mg/l	↑34,2mg/l	↑51.4mg/dL	↑42.40mg/dL	N/R	<10(mg/L)
Procalcitonin	↑0,9ng/mL.	↑0,8ng/mL.	0,415ng/mL.	↑0,12ng/mL.	↑0.5ng/mL	↑0.5ng/mL	0.1 ng/mL	↑<0.5 ng/mL.
Albumin	4,7 g/dl	4,4 g/dl	↓2,4 g/dl	3,16g/dl	↓3.23 g/dL	↓3.275g/dL	↓3.23 g/dL	3.4 a 5.4 g/dl
Inflamatorysmarkers	(Yang et al. 2020)	(Henry et al. 2020) (Lippi y Plebani 2020)	(N. Chen et al. 2020b) (Han et al. 2020)	(Zhang et al. 2020)(N. Chen et al. 2020b)	(T. Chen et al. 2020a)	(C. Wu et al. 2020a)	(Zhou et al. 2020a)	**Normal Values**
Coagulation time	↓9,4 sec	↓7.74sec	↓9,2sec	↓7,5sec	N/R	N/R	N/R	11.0-13,5sec
Thrombin	17,93sec	18,49sec	↓11,3 sec	↓14,3 sec	↓11,3 sec	↓11.10sec	11.6 sec	15-20 sec
Thromboplastin	↓9 sec	41.6sec	↓27,3sec	↑44sec	↑27.3sec	28.70sec	N/R	29.0-42-0 sec
D-Dimer	↑0,59µg/L	↑1,04 µg/L	↑1,2µg/L	↑0,53µg/L	↑0,9µg/mL	↑0,61µg/mL	↑0,8µg/mL	<0.50 (ug/mL)
Ferritin	291.13µg/L	↑1006.16 µg/L	↑808,7µg/L	↑669,7µg/L	↑808,7µg/L	↑594µg/L	↑722µg/L	30-400 µg/L
LDH	↑575,5UI/l	↑512UI/l	↑504UI/l	↑408,1UI/l	↑307.50UI/l	↑336UI/l	↑300UI/l	114-240 UI/l
Fibrinogen	↑5.10g/L	↑4.55g/L	↑4.76g/L	↑5.59g/L	N/R	N/R	N/R	2.0-4.0 g/L
IL-6	3,823pg/mL	3,367pg/mL	↑7,9pg/mL	↑22.0 pg/mL	↑7.9 pg/mL	↑6.98 pg/mL	↑7.4 pg/mL	<7 pg/mL

Discussion.

WHO report 151 confirmed9,473,214 infected cases and 484,249 who have died from SARS-CoV-2. As an emerging virus, many investigations have been carried out to find a treatment and a vaccine to reduce the rate of spread and mortality. but in the face of this adversity, the healthcare personnel have controlled this pandemic, with a correct differential diagnosis and symptomatic treatment (WHO, 2020).

The interpretation of laboratory results are key to determining the patient's clinical status, so a meta-analysis of 26 scientific articles that had relevant information on laboratory test results was performed, of which 10 pieces of research were chosen because these indicated alterations in specific severity markers.In Table # 1, it is possible to see the values (Yang et al. 2020) (Henry et al. 2020) (Lippi y Plebani 2020) (Chen et al. 2020) (Han et al. 2020) (Zhang et al. 2020).

A total of 1,150 patients were determined, most of them male, approximately 60 years old, who presented clinical manifestations such as fever higher than 38 °C, dry cough, rhinitis, flu syndrome, myalgia, and few cases with diarrhea. Patients with comorbidities such as high blood pressure, metabolic disorders such as diabetes mellitus and previous renal, cardiac, and respiratory pathologies had a bad prognosis (Yang et al. 2020).

According to the pathophysiology, dry cough without expectoration is related to alveolar damage, dyspnea with pneumonia, and acute respiratory distress syndrome (ARDS) caused by the storm of pro-inflammatory cytokines (Yang et al. 2020), patients with pleuritic pain is associated with pleural effusion that is observed in tomographies with inflammatory exudate as a result of an acute edema of non-cardiogenic lung (Chen et al. 2020b).

The vast majority of patients presented an increase in immunoglobulin IgM in rapid blood serum tests. In the complete hemogram, a total increase in the concentration of white blood cells was

quantified with a deviation to the left due to neutrophylia and plateletpenia (Zhang et al. 2020), later the chemical biomarkers began to rise due to the multi-organ failure (Chen et al. 2020b).

Approximately, 20% of hospitalized patients who were admitted to the ICU had severe metabolic acidosis, when the patient presented severe pneumonia, the health condition worsened because the viral load increased along with the inflammatory markers, when the virion replicates in the endothelial and vascular cells, it spreads to other organs, causing a multiorgan dysfunction that is confirmed with a leukopenia and a bilateral inflammatory infiltrate that is complicated in respiratory distress (C. Wu et al. 2020a).

These patients had an increase in liver markers such as transaminases (AST, ALT) and lactate dehydrogenase (LDH) greater than 2 times the normal value (C. Wu et al. 2020a)(N. Chen et al. 2020b), and an increase in coagulation times such as thrombin (Tp) and Thromboplastin (Tpp), while patients with cardiac injury presented an increase in TnI cardiac troponin, serum ferritin and CK - MB in addition to proteinemia with values of C-reactive protein higher than (3 times) and slightly increased albumin (Zhou et al. 2020a).

Progressive lymphopenia and a drastic increase in ferritin that exceeds (2 times) its normal value are correlated with cytokine storm, an increase in lactate dehydrogenase (LDH) due to liver damage, while the increase in inflammatory factors such as C-reactive protein, D-dimer twice its standard value (Henry et al. 2020), is due to a procoagulant state, fibrinogen generates thrombi that occludes blood vessels causing ischemia (Yin et al. 2020), whereas patients with heart failure presented thoracic pain and increased TnI troponins.

Patients with renal failure present ureic syndromes such as metabolic acidosis, creatinine increase, Na^+ with high blood pressure urgently needing continuous dialysis therapy (Mohamed et al. 2020).

Intensive care patients dramatically increased ferritin, D - dimer and IL-6 greater than (2 times), as a result of ischemia, atrophy, thrombosis and cell necrosis, these patients presented hepatomegaly

and progressive lymphopenia, due to uncontrolled proliferation of inflammatory cytokines such as interleukins IL-1, IL-6 and tumor necrosis factor (TNF α) (Zhang et al. 2020.), generating a secondary hemophagocytic lymphohistiocytosis (SHLH) (Takami 2020).

The patients with secondary multiorgan dysfunction secondary with septic shock had a double increase in the enzyme lactate dehydrogenase (LDH) and procalcitonin (PCT) due to the exasperated inflammatory response to a bacterial superinfection (Zhang et al. 2020).

It is worth emphasizing that laboratory results are not considered a pathoneumonic marker, but they do help to know the prognosis of the patients and the multi-organ failure.

Control markers for hospitalized patients with SARS-COV-2.

The differential diagnosis of a patient who has contracted COVID-19 begins with Triage, to identify acute respiratory infection. The patient's symptoms are confirmed, characterized by asthenia, myalgias, dysgeusia, hyposmia, flu syndrome, cough dry, dyspnea, fever > 38, in this way it is determined in which phase of the disease the patient is in.

In accordance with the stage of pneumonia, an immunological examination is carried out to determine the concentration of antibodies that the patient produces against the odd agent COVID-19, through the detection of immunoglobulins IgG, IgM, the studies of images are very important such as x-rays and chest MRI to identify pulmonary infiltrates that have to be correlated with an arterial blood gas to verify oxygen saturation and respiratory rate.

Depending on the antibodiestiter, the viral load must be determined by qRT - PCR, identifying the envelope of the E- gene, the nucleocapsid N-gene, and the RdRp gene.

Complementary exams must be performed to know the general condition of the patient such as a complete hemogram, cogulation markers (Thrombin, thromboplastin, Fibrinogen, D-dimer, Interleukin VI), biochemical basic, liver function tests (transaminases, LDH), inflammation markers

(C- reactive protein). If patients presented an alteration of laboratory tests and images, the NEWS gravity scale is used for them to be treated in the ICU (Peberdy Mary Ann et al. 2007).

If the patient presents severe pneumonia with sepsis and secondary multiorgan dysfunction as a result of the exasperated inflammatory response, the patient's severity must be assessed by determining renal markers (Urea, Creatinine, Electrolytes, Total Proteins), cardiac markers (Cardic troponins TnT , TnI , CKMB) and the markers considered poor prognosis (Ferritin, LDH, D-dimer, Interleukin VI, Procalcitonin) that if they increase, they correlate with a septic shock.

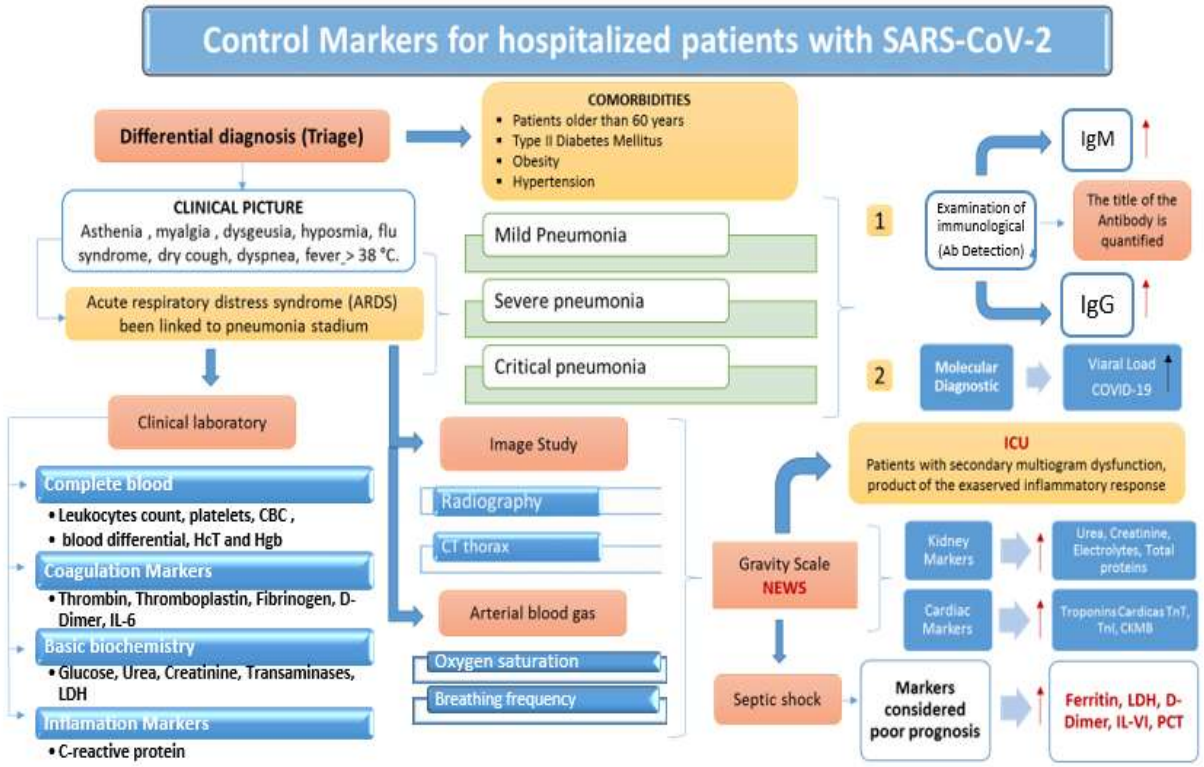

Figure 2. Control Markers for hospitalized patients with SARS-CoV-2.

CONCLUSIONS.

The SARS-CoV-2 infection has a high mortality rate in patients with comorbidities and previous renal, cardiac, and respiratory pathologies. The patients who entered the intensive care unit presented a high viral load that caused sepsis and multiorgan dysfunction.

The prognosis of the patients depends on their immune response since it can be activated uncontrollably, generating macrophage activation with cytokine storms, which are closely related to the increase of inflammatory and coagulation markers.

The most important biomarkers to assess the severity and prognosis of the patient are the Ferritina, D- dimer, LDH, Procalcitonin (PCT) and Interleukin VI. If there is an increase, the patient's mortality is elevated since there is a disseminated intravascular coagulopathy (DIC) and secondary hemophagocytic lymphohistiocytosis (SHLH).

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