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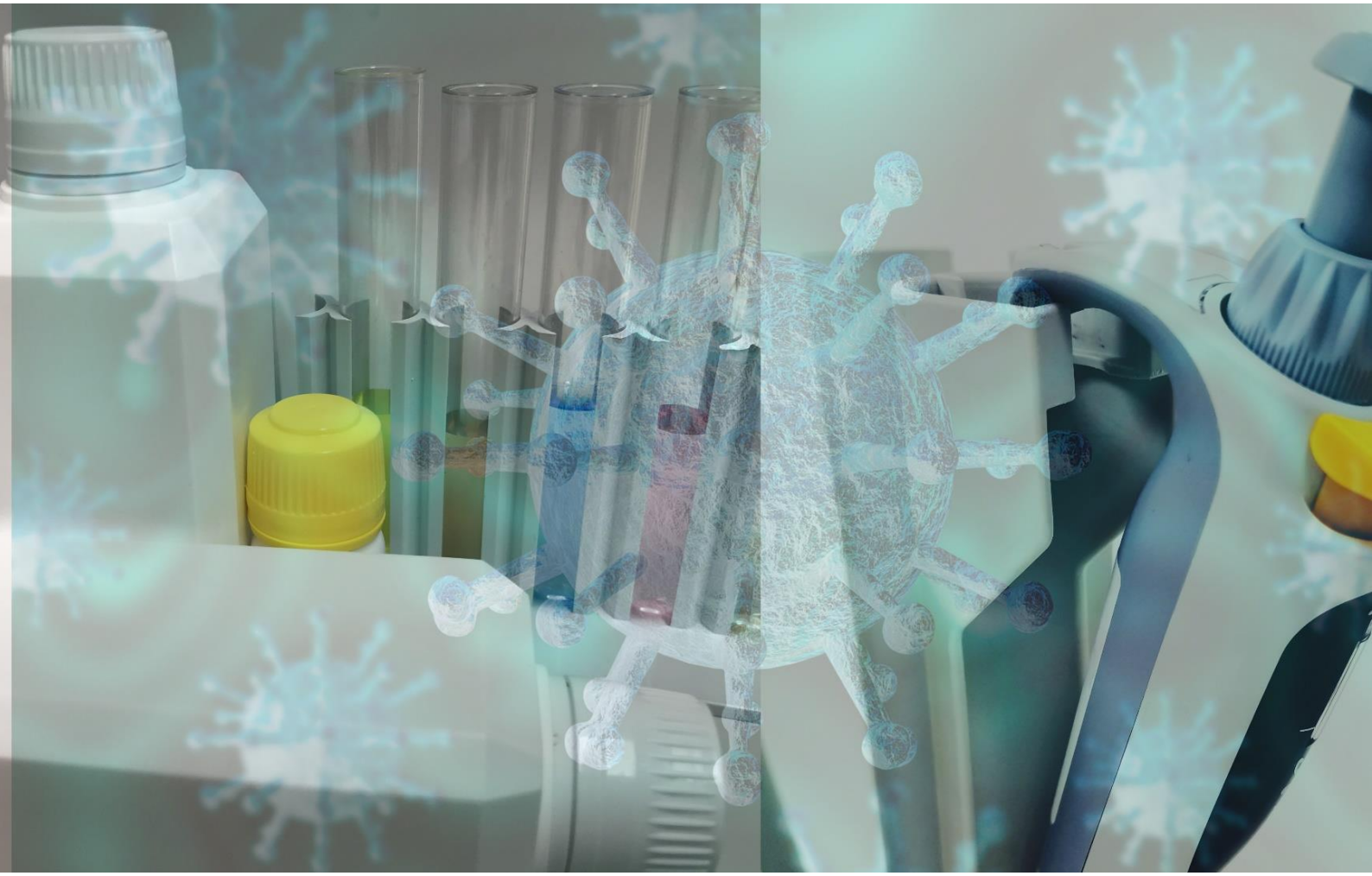

RELATED PARAMETERS ON COVID-19 INFECTED PATIENTS AND ITS MONITORING.

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CHEMELEX S.A.

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MONITORING COVID-19

Dear distributor / user of our products.

At Chemelex we always want to offer the best service to our clients, adapting to their needs, as well as guaranteeing the best quality of both product and service. That is why we feel obliged to offer to our clients a series of indicators that can be altered in early or advanced stages of COVID-19 infection.

Hopefully, then, we made this small guide as a support for professionals dedicatd to in-vitro diagnosis. This based in our accumulated knowledge adquired with other similar infections such as SARS-Cov-2.

As you should already know, Chemelex have a wide range of this reagents and we will try to prioritize all related orders as much as possible.

Kind regards,

Jose Garcia

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Metabolic Function.

The COVID-19 infection causes similar onsets to other pneumonias. Most of the admitted of this disease had increased his **hepatic transaminases**, decreased **albumin levels and kidney failure**.

Another common alteration are **liver function abnormalities** and are more habitual than in other types of pneumonia. Other alterations include increased hepatic transaminases. Other alterations include decreased albumin and kidney failure.

Liver function abnormalities may be more common in patients with COVID-19 compared to other types of pneumonia previously studied.

Zhao D, Yao F, Wang L, et al. A comparative study on the clinical features of COVID-19 pneumonia to other pneumonias. Clin Infect Dis. 2020 Mar 12

To study these indicators, Chemelex offers it's **Biochemistry** line:

Sustrates:

- **Albumin:** One of the most important serum proteins produced in the liver is Albumin. This molecule has an extraordinary wide range rage of functions, including nutrition, maintenance of osmotic pressure and transport of Ca++, Bilirubin, free fatty acid, drugs and steroids. Variation in albumin levels indicate liver diseases malnutrition, skin lesions such as dermatitis and burns or dehydratation.
- **Creatinine:** Creatinine is a waste product result of the normal degradation of the muscles. The Creatinine production depends on the modification of the muscular mass, and it varies little and the levels usually are very stable. With progressive renal insufficiency there is retention in blood of Urea, Creatinine and Uric Acid. Elevate Creatinine level may be indicative of renal insufficiency.

Enzimes:

- **GOT/AST:** The AST is a cellular enzyme, is found in highest concentration in heart muscle, the cells of the liver, the cells of the skeletal muscle and in smaller amounts in other weaves. Although an elevated level of AST in the serum is not specific of the hepatic disease, is used mainly to diagnostic and to verify the course of this disease with other enzymes like ALT and ALP. Also, it is used to control the patients after myocardial infarction, in skeletal muscle disease and others.

- **GPT/ALT:** The ALT is a cellular enzyme, found in highest concentration in liver and kidney. High levels are observed in hepatic disease like hepatitis, diseases of muscles and traumatism, its better application is in the diagnosis of the diseases of the liver. When they are used in conjunction with AST aid in the diagnosis of infarcts in the myocardium, since the value of the ALT stays within the normal limits in the presence of elevated levels of AST.

- **LDH:** Lactate dehydrogenase (LDH) is an enzyme with wide tissue distribution in the body. The higher econcentrations of LDH are found in liver, heart, kidney, skeletal muscle and erythrocytes. Increased levels of the enzyme are found in serum in liver disease, myocardial infarction, renal disease, muscular dystrophy and anemia.

  Between 73% and 76% of patients affected by COVID-19 has increased his concentration of lactate dehydrogenase. As some should know this indicates hepatic injury or erythrocyte lysis and may be more common in patients with COVID-19 compared to other types of pneumonia. This is why LDH may be a considerable marker for evaluation COVID-19.

- **CK-Nac:** Creatine kinase is a cellular enzyme with wide tissue distribution in the body. Its physiological role is associated with adenosine triphosphate (ATP) generation for contractile or transport systems. Elevated CK values are observed in diseases of skeletal muscle and after myocardial infarction. Some studies observe a direct relationship between myocarditis and COVID-19 afection.

TURBIDIMETRY:

- **β2Micro:** β2-m is a protein located on the surface of human lymphocytes and other nucleated cells. Free β2-m is filtered by the glomerulus and subsequently reabsorbed in the proximal tubular cells. Increased urinary excretion of β2-m is a sensitive indicator of **renal insufficiency.**

Zhao D, Yao F, Wang L, et al. A comparative study on the clinical features of COVID-19 pneumonia to other pneumonias. Clin Infect Dis. 2020 Mar 12

- **Ferritine:** Serum ferritin concentration usually reflects body iron stores and is considered one of the most reliable indicators of iron status of patients Whereas low serum concentrations of ferritin are always indicative of an iron deficiency, elevated concentrations can occur for variety of reasons. Thus, although elevated concentrations often indicate an excessive iron intake, they are also caused by liver disease, chronic inflammation and malignancies. Pregnant women, blood donors, hemodialysis patients, adolescents and children are groups particularly at risk.

  Higher levels of Ferritine may be related due the development of cytokine release syndrome.

Mehta P, McAuley DF, Brown M, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet. 2020 Mar 28;395(10229):1033-4

- **CRP:** CRP is an acute-phase protein present in normal serum, which increases significantly after most forms of tissue injuries, bacterial and virus infections, inflammation and malignant neoplasia. During tissue necrosis and inflammation resulting from **microbial infections**, the CRP concentration can rise by more than 300 mg/L in 12-24 h.

  A **high CRP concentration** may be detected in patients with secondary bacterial infection and/or indicate hyper-inflammation. In addition to this, also can use CRP levels to monitor low-dose corticosteroid administration to reduce inflammation.

Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020 Feb 15;395(10223):497-506

COAGULATION:

The first studies of the disease detect **Prothombin time and D-dimer level** (*Parameter Under Development*) on admission were higher in ICU patients than non-ICU patients.

Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020 Feb 15;395(10223):497-506

Another study also showed that non-survivors had significantly **higher D-dimer levels and fibrin degradation product (FDP) levels, longer prothrombin time, and activated partial thromboplastin time compared to survivors.**

Tang N, Li D, Wang X, et al. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost. 2020 Apr;18(4):844-7

Related to this, Chemelex would offer our diagnostic range **Coagulation** products:

- **APTT:** The time measurement of APTT is the most common coagulation procedure performed in routine laboratories, apart from the PT. The APTT is particularly sensitive to defects of the intrinsic coagulation pathway. It is commonly used for monitoring heparin anticoagulant therapy.

- **Fibrinogen:** Fibrinogen (Factor I), protein synthesized by the liver, is the substance used in the blood to form a clot. Its determination is used to evaluate abnormal blood clotting. Elevated Fibrinogen levels are observed in acute inflammations and in pregnancy; low values are observed in **trombolitic therapy, in hepatic disease**, in the congenital non fibrinogen, in DIC (Disseminated Intravascular Coagulation) and in pancreatitis (low values).

- **PT Test:** Since its original description by Quick in 1935, the Protombin Time (PT) or Quick test has remained an important test for detect disorders of blood coagulation, it is the most common coagulation procedure performed in routine laboratories, apart from the APTT. The PT is particularly sensitive to defects of the extrinsic coagulation pathway (Factors II, V, VII, X and fibrinogen) as well as its inhibitors. It is an **indicator of hepatic disease.**

And our range of lyophilized Coagulation Calibrators and Controls:

- **Coagulation CAL:** The calibrator is lyophilised human plasma, containing PT, APTT and Fibrinogen that allows expressing the analytical results in different units as concentration (mg/dL), percentage (%) or activity rate, by manual method.

- **Coagulation Normal Control:** The Control is a lyophilised human plasma, used to evaluate the precision and accuracy of PT, APTT and Fibrinogen determinations in human plasma.
- **Coagulation Path Control:** The Control is a lyophilised human plasma, used to evaluate the precision and accuracy of PT, APTT and Fibrinogen determinations in human plasma.

Other Parameters:

The parameters described above are some of the most related to the COVID-19, but they are other ones that may help monitoring and could be related to the infection of the disease.

- Respiratory function effectiveness is measured by **Blood gases.**

-Macrophage activation may be activated due COVID-19 and it can be observed with the appereance of **Hyperfibrinogenemia.**

-**High PCT levels** are observed in COVID-19 patients. Its presence is non-specific and influenced by factors such as age. An increase in PCT value could indicate secondary bacterial infection.

Note that this document is about to help monitor the evolution of affected patients and does not include direct SARS-CoV-2 virus detection systems or indirect ones based in the study of patient's globulins.

We hope that this document has been of interest and helps you to continue fighting against COVID-19.

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