Contribution to a study of variations in biochemical parameters in COVID-19 patients in the province of Saida.

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Abstract:

Since December 2019, Coronavirus Disease 2019 (COVID-19), caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), emerged in Wuhan and subsequently became a pandemic. Algeria has been severely affected by the virus. COVID-19 affects people in different ways.

The objective of our study is to investigate the direct and indirect complications caused by COVID-19 virus in confirmed patients. The various experimental stages of this project were conducted at Dr. Chouikhi Medical Laboratory in Saida from June 2020 to December 2021, with a total of 1538 patients. This study aims to identify and evaluate the complications of the COVID-19 epidemic in affected individuals and their impact on their health.

Based on clinical and biological data collected from medical records of COVID-19 patients, our results show that this disease exhibits variations in levels of Troponin (<10 ng/ml), CRP (<6), and particularly in D-dimers, which were observed to be higher (greater than 500 ng/ml (<500)) in severe cases compared to non-severe cases. These variations have an impact on biochemical parameters of the liver, kidneys, and lungs. This allows us to understand the effects of COVID-19 on other organs such as the liver and kidneys.

Keywords: Covid-19, liver, kidney, troponin, D-dimers.

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1. Introduction

On December 31, 2019, the WHO office in China was informed of a case of pneumonia of unknown cause discovered in Wuhan, Hubei province. A new type of coronavirus causing this respiratory illness was discovered on January 7, 2020, and is called "SARS-CoV-2". The epidemic continued to spread, and the number of infected individuals increased steadily, initially in China and then in other countries. Most cases were linked to travel from China.

The evolving epidemiology of the COVID-19 coronavirus prompted the WHO Director-General to convene the Emergency Committee on January 22 and 23, 2020. The level of threat associated with COVID-19 at the global level is currently considered to be moderate. On January 30, 2020, following the committee's recommendation, the WHO, through its Director-General, declared the COVID-19 coronavirus outbreak a "public health emergency of international concern" (Direction Générale de la Prévention et de la Promotion de la Santé, 2020).

The virus has spread worldwide and has now become a global pandemic. This epidemic has triggered a health crisis, rapidly spreading across the world, impacting society and the economy, and causing significant disruptions in lifestyles.

The COVID-19 virus responsible for this infection is a novel RNA virus belonging to the family Coronaviridae, completely unknown to human immune memory. Furthermore, it is characterized by its high contagiosity, estimated at 1.4 to 3.8, compared to 1 to 3 for seasonal influenza virus, which explains the rapid spread of the infection worldwide and the high number of infected individuals (Djidjik R., 2020).

The experience of this epidemic shows that we are all exposed to COVID-19 contamination, but not with the same risk of complications. Based on current knowledge, children appear to be less susceptible to pulmonary complications, while patients with chronic diseases, especially those over 60 years old, are more vulnerable. The entire population is at risk of coronavirus

contamination. However, as with many infectious diseases, some individuals are more prone to develop severe complications in case of infection due to their age and health status.

In Algeria, the appearance of this virus was observed on February 27, 2020, starting from an initial outbreak in Blida, with the case being an individual from Europe. The spread of the virus then extended throughout the country (Djidjik R., 2020).

The main objective of this study is to demonstrate the direct and indirect complications caused by the COVID-19 virus in confirmed patients. The aim was to identify the biochemical parameters affected by this virus and monitor their serological variations over time.

2. Materials and Methods

Our study focused on analyzing the immediate and delayed complications caused by the virus responsible for COVID-19 in confirmed patients. To achieve this objective, we followed a rigorous methodology, which included the following steps:

1. Epidemiological survey: We conducted a thorough survey among patients who were diagnosed with the coronavirus during the years 2020 and 2021. This survey aimed to gather detailed information about the symptoms presented by the patients, their severity, the duration of the infection, as well as any complications encountered.

2. Monitoring of biochemical parameters: We performed regular monitoring of patients' biochemical parameters throughout their convalescence. This included blood tests to assess inflammatory markers, liver enzyme levels, white blood cell counts, among others. The objective was to detect any significant variations in these parameters, which could indicate the presence of complications or comorbidities.

3. Control of serological variations: We also conducted periodic serological controls to evaluate the patients' immune response to the virus. This was done by measuring specific COVID-19 antibodies in the patients' blood serum. The variations in these antibody levels over time allowed us to understand the evolution of immunity in patients and assess the risk of reinfection or subsequent complications.

Through this methodological approach, we were able to gather valuable data on the direct and indirect complications associated with the COVID-19 virus. These results contribute to a better understanding of the disease, its short- and long-term consequences, and help guide prevention and treatment efforts to improve the management of patients affected by this infection.

2.1. Experimental Procedure

The experimentation took place at the laboratory of Dr. CHOUIKHI CHEIKH Medical Analysis in Saida, between December 2021 and May 2022. During this period, we conducted biochemical analyses on blood samples collected from the patients.

For blood sampling, we used three different types of tubes: the citrate-containing tube, the heparin-containing tube, and the dry tube. The choice of tube type depended on the specific analysis we wanted to perform later on.

After the collection, the blood samples were centrifuged to separate the various components of the blood. This step allowed us to obtain serum or plasma, from which we performed our analyses.

Depending on the type of analysis to be performed, we used the appropriate tubes. For example, specific tubes were used to measure D-dimers, troponin, or conduct COVID serology. Similarly, the appropriate tube was used to measure C-reactive protein (CRP).

Once the samples were prepared, we subjected them to biochemical analyses within the medical analysis laboratory. These analyses helped evaluate specific parameters related to COVID-19 complications and provided valuable information about the patients' health status.

This process of sampling, centrifugation, and analysis allowed us to obtain important data for our study on COVID-19 complications and contribute to advancing knowledge in this field.

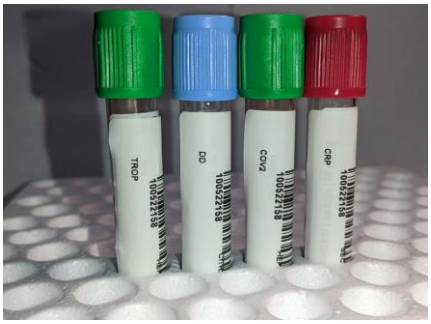

Figure 1. Matériel

Table 1. Type, Color, Quantity of Samples.

Analysis:	**Tube type**	**Tube Color**	**The quantity**
D-dimers	Citrate	Blue	4 mL (mandatory)
Covid Serology	Héparin Plain (or Serum)	Green	2 to 3 mL
CRP (C-reactive protein)	Plain (or Serum) Héparin	Red	2 to 3 mL
Troponin	Héparin	Green	2 to 3 mL

3. Results and Discussion:

During the period from June 2020 to December 2021, our study included a total of 1538 patients, with 601 females and 937 males.

Table 2. Statistics of the year 2020.

Les mois	Serology COVID	Antigenic COVID	D-dimers	CRP	Troponin	female	male
June	60	27	16	60	09	55	57
July	30	47	21	30	02	32	68
August	55	32	18	55	00	63	42
September	09	16	06	09	00	11	20

Table 3. Statistics of the year 2021.

Months	Serology COVID	Antigenic COVID	D-dimers	CRP	Troponin	female	male
January	25	64	10	25	01	36	64
February	13	37	08	13	00	13	45
March	09	25	02	09	00	09	27
April	10	15	00	10	02	11	16
May	05	10	03	05	06	09	15
June	12	40	09	12	00	36	25
July (from July 15th)	66	125	35	66	11	92	145
August	70	150	28	70	15	115	148
September	24	64	10	24	05	40	63
October	09	12	00	09	00	06	15
November	18	53	06	18	04	15	66
December	45	118	14	45	02	58	121

3.1. Variations in COVID antigenic testing

Regarding COVID antigenic testing, we observed that there were between 10 to 150 patients who tested positive. The number of positive cases was high (more than 60 patients) in the months of January, July, August, December, and September (2020), and decreased (less than 60 patients) in the months of July, June, August, September (2020), February, March, April, May, June, October, and November (2021).

These variations can be attributed to several factors:
- Availability of antigenic testing at the laboratory (as it was not widely available in 2020).
- Presence of specific symptoms in patients (such as fever, dry cough, weakness) and the duration of these symptoms (if the duration is within three days, the patient is advised to undergo antigenic testing only, as other COVID tests may not detect the initial infection that occurred in the nasal passage before entering the bloodstream, which explains the inverse relationship between antigenic testing and COVID serology).
- Patient preference for rapid results (as antigenic testing provides results within 20 minutes) (Figure 2).

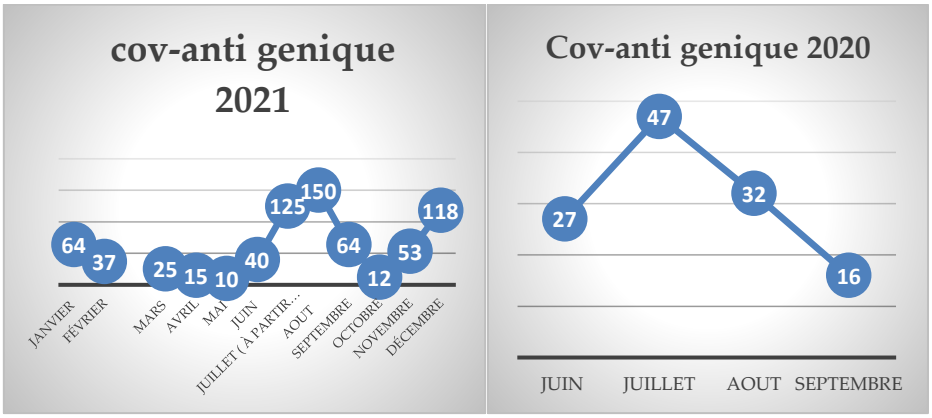

Figure 2. Graphical representation of variations in COVID antigenic testing.

3.2. Variations in COVID serology and CRP (C-reactive protein)

Regarding COVID serology and CRP, we observed that there were between 5 to 70 patients who had a positive result for IGG and IGM levels greater than 1, and CRP levels higher than 6 (>6). This indicates a proportional relationship between them.

The number of positive cases was high (more than 40 patients) in the months of July, August, December (2021), August, and June (2020), and decreased (less than 40 patients) in the months of July, August (2020), February, March, April, May, June, October, November, and September (2021).

These compatible variations can be attributed to:

When a patient's condition worsens and they start showing severe symptoms such as difficulty breathing, chest pain, it indicates that they have progressed beyond the initial stages of the infection, and the doctor requests COVID serology to determine the levels of IGG and IGM, along with a CRP test.
The CRP test helps the doctor to act more quickly and appropriately during the COVID-19 pandemic by distinguishing between severely ill patients and less severely ill patients. (Figure 3)

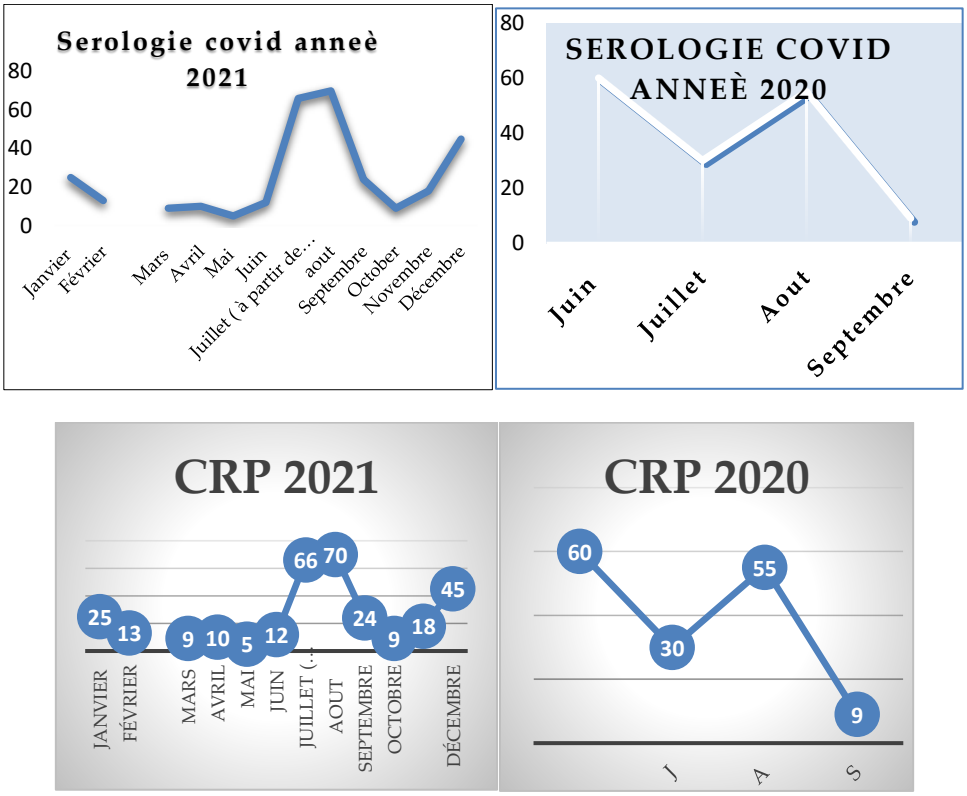

Figure 3: Graphical representation of variations in COVID serology and CRP (C-reactive protein).

3.3. Variations in D-dimer levels

Regarding D-dimer levels, we observed that there were between 0 to 35 patients with D-dimer levels higher than 500 ng/ml (<500).

The number of positive cases was high (more than 10 patients) in the months of January, July, August, December, September (2021), June, July, and August (2020), and decreased (less than 10 patients) in the months of July, August, September (2020), February, March, April, May, June, October, November (2021).

These variations can be attributed to the following:

- During the peak of the COVID-19 epidemic, we noticed a significant elevation of D-dimer levels in patients with severe and critical forms of COVID-19. These patients had plasma concentrations of D-dimers 5 to 10 times higher compared to those found in patients with mild to moderate forms. (Figure 4)

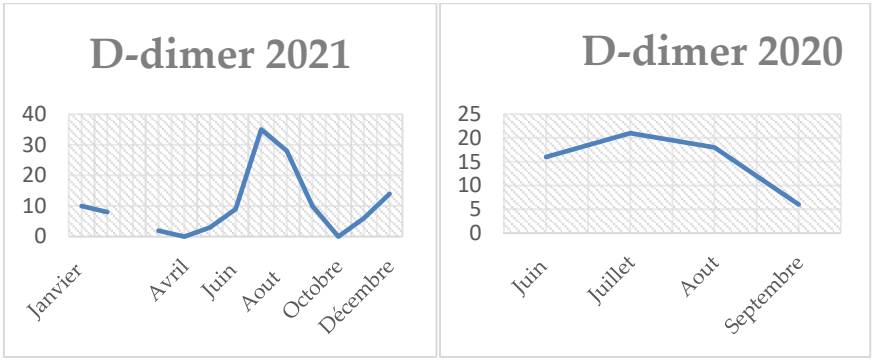

Figure 4: Graphical representation of variations in D-dimer levels.

3.4. Variations in troponin levels

Regarding troponin levels, we observed that there were between 0 to 15 patients with troponin levels higher than 10 ng/ml (<10).

The number of positive cases was high (more than 6 patients) in the months of July, August, May (2021), and June (2020), and decreased (less than 6 patients) in the months of January, February, March, April, June, September, October, November (2021), July, August, September (2020).

These variations can be attributed to the following:

- Cardiac troponin levels can be useful for risk stratification in patients infected with COVID-19.
- Therefore, we observed several cases of COVID-19 with elevated troponin levels. (Figure 5)

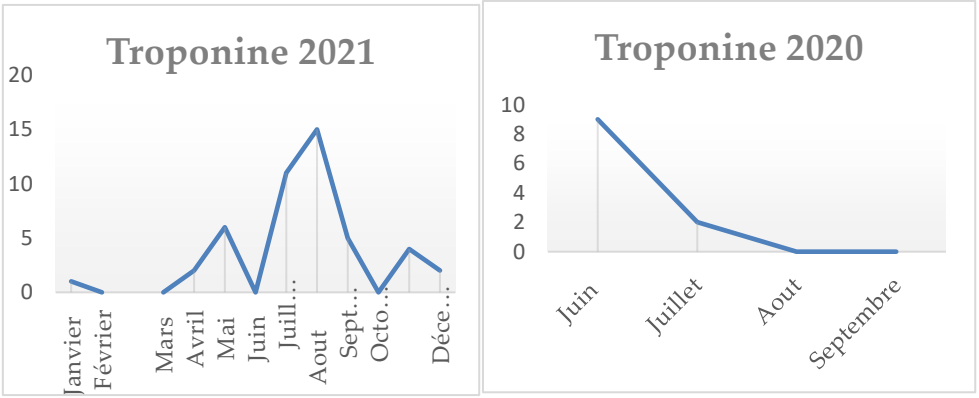

Figure 5: Graphical representation of variations in troponin levels.

Overall, several studies were included in this meta-analysis. The titles, abstracts, and full texts of all identifiable articles based on a search were reviewed, and information on differences in D-dimer values between those reporting COVID-19 patients with or without severe disease was obtained.

There are several parameters that determine whether a patient with COVID-19 requires hospitalization, such as age, presence of other diseases like diabetes, and the patient's immune system status.

Tables 2 and 3 show that the average age of participants is between 35 and 80 years, with male gender being predominant compared to female gender. Comorbidities are present in nearly half of the patients. Hypertension is the most common comorbidity, followed by diabetes, coronary artery disease, and obesity. Indeed, comorbidities are associated with a higher risk of COVID-19.

Table 2 and 3 demonstrate that patients who were not hospitalized had normal D-dimer levels, which did not require hospitalization. On the other hand, hospitalized patients with COVID-19 exhibited higher D-dimer values in severe cases compared to non-severe cases. Although elevated D-dimer levels may indicate a multifactorial etiology and imply a deteriorated health condition requiring hospitalization, our results allow us to conclude that elevated D-dimer levels can be common in severe COVID-19 patients, and a normal D-dimer level indicates that the patient is not in a deteriorated health state and thus may not require hospitalization.

D-dimer testing is primarily performed on elderly subjects or pregnant women who have relatively higher levels. This test helps determine the necessary treatment dosage to administer.

Cohort studies suggest that the incidence of thromboembolic complications in COVID-19 patients ranges from 11% to 35% (Li et al., 2020).

Coagulation disorders such as venous thromboembolism (VTE), ischemic strokes, acute coronary syndrome (ACS) or myocardial infarction (MI), and disseminated intravascular coagulation (DIC) are relatively common in COVID-19 patients, particularly in critical cases with elevated D-dimer levels, requiring continuous vigilance and prompt intervention. Therefore, COVID-19 patients are at high risk of thromboembolic events. Notably, Tang et al. recently highlighted that the majority of COVID-19 patients who died during their hospital stay met the diagnostic criteria for DIC (71.6% vs. 0.6% among survivors) (Tan et al., 2020).

High D-dimer concentrations have also been associated with a higher mortality rate. Zhang et al. reported that a D-dimer concentration above 2.0 µg/mL could predict in-hospital mortality (Zhang et al., 2020). Tang et al. showed that patients who received heparin for more than 7 days had a lower mortality rate compared to those who did not receive anticoagulation (Tan et al.,

2020), suggesting that early and prolonged antithrombotic treatments such as anticoagulants or antithrombins may be beneficial for severe cases of COVID-19.

However, D-dimer testing remains a monitoring test rather than a diagnostic test for COVID-19 patients. It provides prognostic value and can guide care based on the risk of thromboembolic complications, but additional tests are necessary to confirm the diagnosis. In fact, D-dimer testing is highly sensitive but lacks specificity, as it can detect small amounts of fibrin that form in various situations (infection, inflammation, pregnancy, etc.). It yields a high rate of false positives. Demelo-Rodríguez et al. demonstrated in their study of 156 COVID-19 patients who underwent D-dimer testing that the sensitivity of the test was 95.7%, and the specificity was 29.3% (Demelo-Rodríguez et al., 2020). Yao et al. also showed in their study of 248 COVID-19 cases that D-dimers had a sensitivity of 83.3% and a specificity of 71.3% (Y. Yao et al., 2020). Gao et al.'s studies on a population of 43 COVID-19 cases demonstrated that D-dimer had a sensitivity of 93.3% and a specificity of 75.0% (Y. Gao et al., 2020).Previously, the lack of specificity was considered a drawback of D-dimer testing.This meta-analysis

Conclusion

COVID-19 is an infectious disease caused by the novel SARS-CoV-2 virus, which spreads worldwide and is transmitted directly or indirectly between people. The Saida province is among the provinces in Algeria affected by the pandemic, which prompted this study to determine the detection methods (types of tests) and the parameters affected by COVID-19 in Saida.

The detection methods for COVID-19 in Saida are based on an antigenic COVID-19 self-test conducted at private laboratories (such as the medical analysis laboratory of Dr. Chouikhi Cheikh) after a nasopharyngeal swab. Serological testing (IGG-IGM) is also performed after a blood sample.

The results of these tests show that men are more affected than women (60% vs. 40%), and according to the laboratory where this study was conducted, 1538 cases are infected. The actual level of COVID-19 contamination is often underestimated because a large number of infected individuals are not detected by this laboratory. Additionally, Saida is the most affected Daïra by this virus due to a lack of compliance with precautionary measures. Therefore, it is important to follow hygiene measures to protect one self and others.

Vaccination against COVID-19 is also a preventive measure and helps reduce severe disease complications, deaths, and the incidence of the virus, thus minimizing its spread in the population.

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