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# Comparative Analysis of Biochemical Indexes of Severe and Non-Severe Patients Infected with COVID-19

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## Abstract

**Background:** The coronavirus disease 19 (COVID-19) is a highly transmittable and pathogenic viral infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The characteristics of laboratory findings of coronavirus are of great significance for clinical diagnosis and treatment. This study aimed to evaluate the accuracy of biochemical parameters in COVID-19 and to compare them according to the severity of the disease.

**Methods:** This diagnostic accuracy study was conducted in COVID-19 patients, During the study period 169 COVID-19 patients were hospitalized at the Avicenne military hospital, 20 patients in the medical intensive care unit (severe group) and 149 patients in the COVID-19 isolation hospital (non-severe group).

**Results:** Through the analysis of laboratory data of patients with COVID-19 (169 patients), we demonstrated that severe cases possessed higher levels of C-Reactive Protein (CRP), Aspartate Aminotransferase(AST), Alanine Aminotransferase (ALT), and Urea levels in serum, creatinine, hypoalbuminemia, hyponatremia, hyperbilirubinemia, troponin, procalcitonin.

**Conclusion:** The analysis of the current scientific literature demonstrates the value of laboratory parameters as simple, rapid, and cost-effective biomarkers in COVID-19 patients.

**Keywords:** COVID-19; Laboratory data; Severe cases

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## Introduction

Coronaviruses are RNA viruses, found widely in humans, mammals, birds and bats. These viruses can cause infections of the respiratory tract, gastrointestinal system and nervous system [1-3]. In December 2019, a new coronavirus was identified in the city of Wuhan, province of Hubei in China, in patients with severe unexplained pneumonia [1].

In February 2020, the World Health Organization (WHO) assigned the name COVID-19 to designate the disease caused by this virus, initially called 2019-nCoV, then SARS-CoV-2 by the International Committee on Taxonomy of Viruses [4]. After SARS-CoV-1 in 2002 in China, then MERS-CoV in 2012 in the Arabian Peninsula responsible for often fatal respiratory distress syndromes, it is the third threat for global public health linked to a coronavirus in less than twenty years [5]. The clinical features of severe COVID-19 are similar to those of severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) COVID-19 behaves differently. It has a more rapid transmission and longer incubation period both of which adds to the woe of disease containment.

The aim of our study was to describe the biochemical disturbances of SARS-CoV-2 infection in a sample of patients and to compare these disturbances according to the severity of the infection.

## Patients and Methods

This is a prospective comparative study, spread over a period of 4 months (March 2020-June 2020) of the biochemical disturbances of COVID-19 patients admitted to the Avicenne Military Hospital.

The COVID-19 diagnosis was suspected according to WHO recommendations [6], and confirmation of the presence of SARS-CoV 2 was made by PCR-RT (Polymerase Chain Reaction- Real

Time) [7] and the Pneumonia Severity Index (PSI) and CURB-65 scores were calculated as suggested in the literature [8].

During the study period 169 COVID-19 patients were hospitalized at the Avicenne military hospital, 20 patients in the medical intensive care unit (severe group) and 149 patients in the COVID-19 isolation hospital (non-severe group).

Each patient received, upon admission, a sample of five millilitres of whole blood on a dry tube, centrifuged at 3000 rpm for five minutes. The biochemical parameters were determined by chemiluminescence method using the Cobas Roche multiparametric analyzer.

All the patients underwent a biochemical indexes: Assessment of Liver Function (AST, ALT, LDH, bilrubin, albumin), renal function (urea, creatinine), Inflammatory Biomarkers Examination (CRP, ferritinemia, pro calcitonin), blood ionogram, Cardiac markers (High-Sensitivity Troponin T).

## Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics V21.0. Quantitative variables are expressed as median and mean and Fisher's test was used for analysis of qualitative variables. We considered a *P*-value less than 0.05 as statistically significant.

# Results

## Patients

During the study period 169 COVID-19 patients were hospitalized at the Avicenne military hospital, 20 patients in the medical intensive care unit (severe group) and 149 patients in the COVID-19 isolation hospital (non-severe group). The median age in patients was 43 (19-93 years), the 30-50 years age group accounted for 65% of patients. Males represented 90% of the study population. Thirty two patients presented with one or more co-morbidities, hypertension and diabetes mellitus was the commonest of comorbidities **Table 1.**

## Biochemical disturbances

The biochemical disturbances observed in our series with comparison between the 2 groups of patients have been listed in **Table 2.**

**Table 1** Clinical characteristics of patients with COVID-19 severity (Severe versus non-severe).

| Characteristics | Total (n=169) | Disease severity | | P-value |
|---|---|---|---|---|
| | | Severe (n=20) | Non-severe (n=149) | |
| Median age | 43 years (19-93) | 44 years (41-83) | 43 years (19-93) | |
| **Sex** | | | | |
| Male | 153 (90%) | 18 (12%) | 135 (88%) | 1 |
| Female | 16 (10%) | 2 (12%) | 14 (88%) | |
| **Comorbidities** | | | | |
| Diabetes | 14 (8%) | 12 (86%) | 2 (14%) | <0.001 |
| Arterial hypertension | 18 (11%) | 14 (78%) | 4 (22%) | <0.001 |
| Renal failure | 7 (4%) | 6 (86%) | 1 (14%) | <0.001 |
| Hepatic insufficiency | 4 (2%) | 3 (75%) | 1 (25%) | 0.005 |
| Others | 2 (1%) | 2 (100%) | 0 (0%) | 0.01 |

**Table 2** Association of abnormal biochemical test results with COVID-19 severity (Severe versus non-severe).

| Characteristics | Reference values | Total (n=169) | Disease severity | | P-value |
|---|---|---|---|---|---|
| | | | Severe (n=20) | Non severe (n=149) | |
| CRP (mg/L) | < 5 | 66 (35%) | 16 (20%) | 50 (33%) | 0.001 |
| AST (U/L) | < 50 | 10 (6%) | 5 (25%) | 5 (3%) | 0.002 |
| ALT (U/L) | < 65 | 14 (8%) | 8 (40%) | 6 (4%) | <0.001 |
| Hyponatremia (mmol/L) | 136-145 | 17 (10%) | 6 (30%) | 11 (7%) | 0.006 |
| Hyperkalemia (mmol/L) | 3.5-4.6 | 4 (2%) | 2 (10%) | 2 (1%) | 0.07 |
| Hypochloremia (mmol/L) | 97-109 | 16 (9%) | 4 (20%) | 12 (8%) | 0.1 |
| Hypoalbuminemia (g/L) | 35-50 | 10 (6%) | 9 (45%) | 1 (0%) | <0.001 |
| Urea (mmol/L) | 2.50- 7.50 | 13 (8%) | 10 (50%) | 3 (2%) | <0.001 |
| Creatinine (µmol/L) | 60-120 | 21 (12%) | 14 (70%) | 7 (5%) | <0.001 |
| LDH (U/l) | 135-225 | 55 (32%) | 10 (50%) | 45 (30%) | 0.12 |
| hyperbilrubinemia (µmol/L) | <17 | 7 (4%) | 4 (20%) | 3 (2%) | 0,004 |
| High-sensitivity cardiac troponin T (ng/mL) | <0.014 | 5 (3%) | 5 (25%) | 0 (0%) | <0.001 |
| Procalcitonin (ng/mL) | 0.5 | 20 (13%) | 14 (70%) | 6 (4%) | <0.001 |
| Hyperferritinemia (ng/mL) | 30-400 | 23 (14%) | 6 (30%) | 17 (11%) | 0.03 |

### Inflammatory biomarkers examination

Increased C-reactive protein (CRP) concentration appeared in 35% [105 mg/L (25-224) *vs.* 43 mg/L (7-14), p =0.001] , pro calcitonin (PCT) increased in 13% [1.66 ng/mL (0.61 - 4.75) *vs.* 0.88 mg/l (0.51-1.0), p <0, 001] and hyper-ferritnemia 14% [1777 µg/L (662 - 2000 ) *vs.* 800 µg/L (551-1200), p =0. 03].

### Liver function

With COVID-19 has been observed an increase of AST in 6% [207 U/L (64 - 616) *vs.* 171 U/L (56-344), p=0.002], ALT in 8% [323 U/L (103-1271) *vs.* 242 U/L (77-201), p <0.001], LDH 32% [341 U/L (230-864) *vs.* 326 U/L (236-352), p =0.012], hyperbilrubinemia 7 4% [26 µmol/L (16-52) *vs.* 22 µmol/L (20-25), p =0.004].

### Renal function

The increase in creatinine 12% [261 µmol/L (124-433) *vs.* 201 µmol/L (84-488), p<0. 001], urea 8% [20 mmol/L (8.6-35) *vs.* 18.6 mmol/L (7.8-71), p <0.001] were observed among the included patients with COVID-19. Besides, albumin reduction in 6% [26 g/L (21-30) *vs.* 33 g/L (31-35), p<0.001].

### Blood electrolytes

Hyponatremia was detected in 10% [129 mmol/L (125-130) *vs.* 132 mmol/l (129-134), p=0,006], hyperkalemia 2% [5 mmol/L (4.6-6.1) *vs.* 4.9 mmol/L (4.7-5.9), p=0.07], hypochloremia 9% [92 mmol/L (85-95) *vs.* 92 mmol/L (89-96), p=0.1].

### Cardiac markers examination

High-Sensitivity Troponin T testing was positive in 3%, all patients was from the severe group.

## Discussion

The objective of our work was to report the different biochemical disturbances associated with COVID 19 infection and to compare them according to the severity of the infection between 2 groups of patients.

In our study patients in the severe group had more comorbidities, especially diabetes and hypertension. Most studies reported higher morbidity and mortality with covid-19 among patients with co-morbid conditions [9-11].

High infection-related biomarkers (PCT, CRP) have been observed in our study, an increase in CRP was observed in 66% of patients and 80% of patients in the intensive care unit. The CRP is a good predictor of adverse consequences and related to inflammation of tissues and organs [9-11]. A simple death risk index (ACP) consisting of age and CRP was developed by Lu et al. [11], by which the short-term mortality associated with COVID-19 can be predicted. Higher serum hypersensitive C-reactive protein (hs-CRP) is an important marker of poor prognosis in COVID-19 patients and can be used to predict the risk of death in severe patients, which reflects the persistent state of inflammation [12].

In term of biochemical indicators, patients with organ dysfunction, (including ARDS, acute renal injury, heart injury, liver dysfunction, pneumothorax, etc.) are prone to exhibit abnormal results of blood biochemical examination [13]. In numerous reports, serum ferritin and D-dimer levels are established to be higher in patients with severe COVID-19 than those with a mild clinical picture [14-16].

Increased LDH levels, ASAT/ALAT ratio, total bilirubin could be identified as predictors of liver damage and were positively correlated with the risk of death in COVID-19 patients [17,18].

Two recent studies have shown that the angiotensin converting enzyme 2 (ACE 2) was the primary receptor for SARS-CoV-2 for entry into cells [19,20], which was mainly localized in the heart , kidneys and testes, and expressed weakly in other tissues, particularly in the colon and lung [21]. Another recent study showed that SARS-CoV-2 could bind directly to positive cholangiocytes (ECA2) and cause liver damage [22], which may partly explain the contribution of SARS-CoV-2 infection to hepatic dysfunction. Additionally, the use of ACE inhibitors and angiotensin II receptor inhibitors (ARBs) may also affect liver tests [23].

Albumin, urea, and creatinine were risk factors in assessing kidney damage and disease progression [24].

Many patients had an abnormal urinalysis on admission, including proteinuria or hematuria, indicating that urinalysis may better reveal the potential risk of kidney damage in COVID-19 patients and predict the outcome and severity of the disease [25-28].

In short, cardiac biomarkers, examination of liver and kidney function in severe COVID-19 patients; can assess the degree of extra-pulmonary complications [29]. In addition, electrolyte blood disturbances are of great importance for patients with underlying diseases including disorders of electrolyte balance and glucose metabolism [30].

Furthermore, the level of lactic acid, plasma angiotensin II, amylase and lipase can also be used as indicators to estimate the course of the disease [31,32]. Plasma angiotensin II level linearly correlated with virus titer and the degree of lung injury was increased in one study [33]. Other than the high expression of Angiotensin-converting enzyme 2 (ACE2) in the pancreatic tissue of COVID-19 patients, the increase of serum amylase and lipase were found [34].

## Conclusion

Based on the results of this study, we conclude that CRP, ALAT, ASAT, Urea, Creatinine, Troponin and Procalcitonin have very good accuracy in predicting the severity of COVID-19 infection. Our study also found that severe COVID-19 cases occurred mostly in older people with co-morbid conditions like hypertension, diabetes and cancer. Despite the limitations, the analysis of the current scientific literature demonstrates the value of laboratory parameters as simple, rapid, and cost-effective biomarkers in COVID-19 patients.

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