



Analysis of Biochemical Markers in COVID-19 Patients

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Abstract

Background: Global health emergency COVID-19 is caused by the SARSCoV-2 virus. Present studies explain the alteration in biochemical and immunological parameters, that become useful to clinical condition of COVID-19 patient. The total of 100 COVID-19 patients were included in the final analysis at AIMSRS, Udaipur, Rajasthan.

Materials and Method: This paper focuses on analyzing the importance of biochemical biomarkers including D-Dimer, LDH, IL-6 and CRP in COVID-19 patients and their implications in the evolution of the disease by using standard procedure of selected biochemical parameters.

Results: The increased high-sensitivity C-reactive protein (hs-CRP) can serve to distinguish between patients suspected of presenting COVID-19. Moreover, elevated LDH is one of the most frequently altered biochemical parameters on admission and the increase of certain inflammatory cytokines (IL-6) can contribute information to the follow-up of the disease.

Conclusion: This meta-analysis showed that higher serum CRP, D-dimer levels were observed and there is a significant elevation of inflammatory cytokines IL-6 and LDH also were associated with a composite poor outcome in patients with COVID-19.

Keywords: COVID-19, D-Dimer, LDH, IL-6 and CRP

Introduction

The coronavirus disease (COVID-19) is caused by the severe acute respiratory syndrome (SARS-CoV-2) [1], which spread globally and was declared by pandemic by WHO on 11 March 2020 [2]. The spikes (S) glycoproteins of the virus act as binding proteins and allow the entry of this virus into the target cell of lungs. Protein S is trimeric, that interacts with the target cell and binds with an ACE2 domain [3].

COVID-19 is diagnosed through laboratory tests in patients with epidemiological history and clinical symptoms, together with radiological examinations [4; 5]. The COVID-19 disease has different clinical presentations, ranging from asymptomatic to mild,

moderate, or severe symptoms, with or without the presence of pneumonia [6].

The accumulated evidence has shown that many biochemical parameters become altered in COVID-19 patients, and this has been correlated with the severity of the disease and in some cases associated with the prognosis of the patients. The laboratory parameters together with other demographic and clinical data of patients could allow them to be categorized in the initial stages, thus identifying people who will become critically ill and making it possible to improve their clinical care and seek adequate therapeutic strategies. Clinical laboratories play an essential role in the detection of the virus as well as to the follow-up of patients (monitoring their

evolution) and epidemiological surveillance via the determination of serological markers in their systems [7].

Some parameters for which an unfavorable course of the disease has been described are absolute neutrophilia, the elevation of liver enzymes, creatinine, and nonspecific inflammatory markers such as C-reactive protein (CRP) and Interleukin 6 (IL-6) [9]. Notwithstanding the above, the main progression predictors described are lymphopenia, elevated D-dimer, although it is also necessary to consider LDH, CPK and troponin in the marker panel [10]. This paper focuses on analyzing the importance of biochemical biomarkers including D-Dimer, LDH, IL-6 and CRP in COVID-19 patients and their implications in the evolution of the disease.

Materials And Methods

A study was conducted in Pacific Institute of Medical Sciences, and Ananta Institute of Medical Science & Research Centre, Rajsamand, Rajasthan, from January to June 2021 on COVID-19 patients. The source population was all cases of COVID-19 admitted at AIMSRC with a confirmed diagnosis of COVID-19 using RT-PCR, as reported by central laboratory. All consecutively admitted Severe COVID-19 patients during the Six months follow up period with complete baseline clinical and laboratory data and outcome data were included in the study. With these criteria, a total of 100 COVID-19 patients were included in the final analysis.

Pediatric and pregnant patients, patients with history of head trauma, preexisting smell and taste alterations for any other reason, allergic rhinitis and chronic rhinosinusitis based on clinical history and CT findings were excluded.

Clinical Methodology

Symptoms (fever, cough, dyspnea, headache, nasal congestion, rhinorrhea), serum IL-6 levels, C-reactive protein (CRP), D-dimer, lactic acid dehydrogenase (LDH) levels) were recorded by using Autoanalyzer.

Statistical Analysis

For the quantitative analysis, we used the software SPSS software. In this meta-analysis, all p values reported were two-tailed with the statistical significance set at ≤ 0.05 .

Results

A statistically significant difference was detected for variables with a P-value of < 0.05 . Variables significantly associated with disease severity at 25% level of significance in the univariate analysis were considered in the multivariable model.

In a study where the levels of C-reactive protein in COVID-19 patients were evaluated. Moreover, Liu et al[14] established that the C-reactive protein was significantly higher in the progression group than in the recovery/stabilization group (38.9 vs. 10.6 mg/L).

Furthermore, it has been reported that the elevation of the lactate dehydrogenase enzyme (LDH) used as a marker of lung tissue damage, is one of the most frequent biochemical anomalies in COVID-19 patients on admission to the hospital [7]. Many studies have shown that patients with mild infection have LDH values within the reference ranges, unlike patients in critical condition [11, 12], where a significant difference in the magnitude of the alteration is observed in the seriously ill patients [13].

Table 1. Laboratory parameters related to inflammation on admission of patients diagnosed with COVID-19, according to the severity of the disease[11]

| Parameter | No of cases | Reference range (U/L) | <i>P value</i> | |
|-----------------------------|-------------|-----------------------|----------------|-------------|
| Lactate dehydrogenase (U/l) | 52 | 120–240 | 0.205 | Significant |
| | 42 | 115–245 | 0.205 | – |
| | 16 | ≤ 245 | 0.203 | Significant |
| | 12 | 110–235 | 0.200 | – |

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|---------------------------|----|---------|-------|-------------|
| | 17 | 115–245 | 0.200 | – |
| C-reactive protein (mg/l) | 49 | 0–5.0 | 0.167 | – |
| | 14 | <05 | 0.160 | – |
| | 16 | 0–4 | 0.161 | – |
| | 53 | 0–5 | 0.159 | Significant |
| | 49 | 0–1.0 | 0.158 | Significant |
| D-Dimer (ng/ml) | 49 | <0.05 | 0.097 | Significant |
| | 39 | 0–5.0 | 0.092 | – |
| | 27 | <0.1 | 0.096 | – |
| | 10 | 0–0.5 | 0.097 | – |
| | 39 | 0–5 | 0.092 | Significant |
| | 54 | 0–0.05 | 0.090 | Significant |
| Interleukin-6 (pg/ml) | 39 | 0–7 | 0.026 | – |
| | 6 | 0–7 | 0.026 | Significant |
| | 56 | 0–7 | 0.024 | Significant |
| | 34 | 0–7 | 0.020 | - |

Yuan *et al* [15] revealed that in the first six days of hospitalization, those patients in severe clinical conditions showed significantly higher levels of IL-6 and LDH in serum than those of the moderate group. Interestingly, the decrease of serum levels of LDH and CK was correlated with the elimination of viral mRNA, suggesting that the constitutive reduction in the levels of LDH or CK is likely to predict a favorable response to the course of infection in COVID-19 patients [15].

In the univariate analysis, it was possible to associate it with a greater probability of in-hospital death in patients with elevated LDH, IL-6 and procalcitonin [16], where it was observed that LDH increases in both groups (survivors and non-survivors) in the early stage of the disease, but in this study decreased as of day 13 in the survivors [16].

Discussion

COVID-19 constitutes a major public health problem at a global level and is related to multiple complications that affect both the health of patients and the associated health care costs. For this reason, clinical laboratories can contribute to establishing

biomarkers that would make it possible to stratify the risk of patients evolving toward more serious conditions, thus expediting clinical decision making [12]. Although predisposing factors have been defined (gender, risk ages and association with pathologies such as obesity, diabetes, and hypertension) [16], it is fundamental to use biomarkers that would allow a distinction to be made regarding the progression of the disease and anticipate which patients could require advanced medical procedures, thus making possible a focalized use of clinical resources.

The combination of eosinopenia and increased high-sensitivity C-reactive protein (hs-CRP) can serve to distinguish between patients suspected of presenting COVID-19 (supporting the diagnostic process) from patients with pneumonia or a respiratory infection like COVID-19 [17]. Moreover, elevated LDH is one of the most frequently altered biochemical parameters on admission [7] and the increase of certain inflammatory cytokines (IL-6) can contribute information to the follow-up of the disease (Table 1).

Interestingly, the use of other analytical technologies such as proteomic studies has enhanced the

identification of potential biomarkers that express differentially depending on the severity of the clinical condition of COVID-19 patients, which include factors of the complement, coagulation factors, modulators of inflammation and pro-inflammatory factors. These findings, as a complement to the variations in classic laboratory parameters, could contribute to identify potential therapeutic targets against infectious agents [18].

Conclusion

Clinical laboratories play a pivotal role in the SARS-CoV-2 pandemic, not only from a diagnostic point of view but also in terms of the prognosis of COVID-19 patients. This meta-analysis showed that higher serum CRP, D-dimer levels were observed and there is a significant elevation of inflammatory cytokines IL-6 and LDH also were associated with a composite poor outcome in patients with COVID-19.

Ethical Issues

Research project approved by the ethics committee of Pacific Institute of Medical Sciences, and Ananta Institute of Medical Science & Research Centre, Udaipur- 313003, Rajasthan, INDIA.

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