



Prognostic Value of Elevated Lactate Dehydrogenase and C-Reactive Protein In Covid-19 Patients: A Case-Control Study.

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ABSTRACT

Aim & objectives: The aim of this study is to estimate the levels of Serum LDH and C-Reactive protein in COVID-19 patients and healthy controls.

Materials and Methods: In this study, 50 COVID-19 patients and 50 healthy controls of both gender matching in age and sex were included. The analysis of biochemical parameters was done by using autoanalyzer using diagnostic reagent kit.

Results: In the present study Mean of Serum LDH and CRP was higher in COVID-19 patients than controls. ($P < 0.001$)

Conclusion: Significant changes were observed in Serum LDH and C - reactive protein. They are favorable prognostic biomarkers with high accuracy for predicting the in-hospital mortality in patients with COVID-19.

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I. INTRODUCTION

As of March 9, 2020, more than 100,000 cases of coronavirus disease-2019 (COVID-19) were reported in more than 100 countries with thousands deaths globally. It is now known that Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) is a new type of coronavirus causing COVID-19 infection.[1] COVID-19 is one of the most common diseases, and the trend is rapidly increasing. It has infected 65.8 million people globally, resulting in over 1.5 million deaths[2] Even through most of the patients with COVID-19 is only mildly symptomatic, a notable proportion of patients deteriorate remarkably, causing multiple organ failure that result in death.[3] Cost-effective biomarkers, especially those that are routinely tested, enable risk stratification to allow prudent resource allocation.[4]

Lactate dehydrogenase (LDH) is a cytoplasmic enzyme which is widely expressed in tissues. The enzyme catalyzes the interconversion of pyruvate and lactate with concomitant interconversion of NADH and NAD⁺. [5] LDH comprises two separately enclosed subunits, resulting in five isoenzymes. Each enzyme is expressed in a specific organ: LDH 1 in cardiomyocytes, LDH 3 in lung tissue and LDH 5 in hepatocytes.[6,7] Increased LDH was observed in different conditions such as tissue injury, necrosis, hypoxia, hemolysis or malignancies.[7,9]

Coronavirus disease 2019 (COVID-19) is a disease that could cause multiple organ injuries including heart, Liver and kidney injuries.[9-12] Similarly, a growing number of studies demonstrated that elevated LDH value was associated with significantly increased mortality in patients with COVID-19. [13,14]

CRP is an acute phase, nonspecific marker of inflammation or infection and has been found to broadly correlate with disease severity and treatment response across a variety of infectious and noninfectious conditions. Elevated CRP levels have been previously reported in severe acute respiratory syndrome, Middle East respiratory syndrome, H1N1 influenza.

Recent studies have reported that CRP level is elevated in patients with COVID-19 and may correlate with severity of disease and disease progression.[15]

However, a small subset of non-severe patients will develop into severe cases. In order to identify this group of patients early and actively monitor and treat them is critical to reducing mortality and improving outcome of COVID-19 patients. In view of our study aimed to investigate serum LDH and CRP levels in COVID-19 patients and compared with healthy controls.

II. MATERIAL AND METHODS:-

This study was carried out on COVID-19 patients admitted in Shivtej Arogya Seva Sanstha's Govt. COVID care center. Fifty patients with confirmed COVID-19 according to ICMR and fifty healthy age and sex matched non-COVID-19 controls were included in the study after obtaining their informed consent. The study was conducted on with age group between 20 to 60 years. The analysis of biochemical parameters was done using standard grade reagent chemicals. Serum Lactate Dehydrogenase and C-reactive protein were assayed by autoanalyzer using diagnostic reagent kit.

The exclusion criteria included subjects of any systemic or metabolic disease, liver disease, vascular diseases, renal artery stenosis, alcoholics, pregnant female and those who were taking any kind of medication last few years. A record was maintained containing current history, diet along with laboratory investigations and previous history of any disease.

LDH enzyme assay was analyzed using UV Kinetic decreasing reaction optimized DGKC method.[16] CRP was analyzed using Immunoturbidimetry method. [17]

DISTRIBUTION OF STUDY SUBJECTS:

| | |
|-----------------|---------------------------|
| Group I | N = 50 COVID-19 patients. |
| Group II | N= 50 Healthy controls |

COLLECTION OF BLOOD SAMPLES:

Blood was collected from each subject under aseptic conditions by using vacutainers. The blood samples were allowed to clot at room temperature for 20–30 minutes & serum was separated from cells by centrifugation for analysis of biochemical parameters. The analysis of biochemical parameters were done by using standard grade reagents and chemicals. Serum reagent as per the manual provided by the manufacturer.

III. RESULTS

Table no. 1 : The mean value of Serum LDH , CRP in COVID-19 patients and controls.

| Name Of The Parameters | Covid-19 Patients (N=50) | | Controls (N=50) | | Significance |
|------------------------|--------------------------|--------------------|-----------------|--------------------|----------------------|
| | Mean ±SD | Std. Error of Mean | Mean ±SD | Std. Error of Mean | |
| LDH | 585.16±139.75 *** | 19.76 | 296.28±57.61 | 8.14 | P = 0.001 |
| CRP | 11.10±19.60 *** | 2.77 | 0.82±0.15 | 0.02 | P = <0.001 |

The statistical method used to compare data was unpaired 't' test

*P> 0.05.....Not Significant

**P<0.05.....Significant

***P<0.001.....Highly Significant

There is highly statistically significant difference in means of serum LDH and CRP (P < 0.001) as compared to controls.

IV. DISCUSSION

Our study examined the levels of LDH and CRP which showed highly significant (P < 0.001) values in COVID-19 patients compared to controls. Similar report has been reported by Erika Poggiali et al. showing increased LDH and CRP level in 89% and 98% respectively in COVID-19 patients. [18] It is also in agreement with other studies [19,20] showing increased CRP levels.

LDH is an enzyme involved in energy production by conversion of lactate to pyruvate and it is present in almost all body cells with highest levels in heart, liver, lungs, muscles, kidneys and blood cells. LDH is a general indicator of acute or chronic tissue damage and is considered an inflammatory marker.[21] LDH has been described to be increased during acute and severe lung damage, and an elevated LDH value has been found in other interstitial lung infections.[22] CRP is a reliable marker of acute inflammation. CRP is a hepatic protein regulated at the transcriptional level by the cytokine IL-6 and IL-1.[23]

In emerging literature, ARDS in CoVID-19 patients has been related to a systemic hyper-inflammation or cytokine storm, sustained by IL-6 and IL-1 increase [24], and multiple trials are ongoing on anti-cytokine therapy .[25]

In COVID-19 patients, LDH and CRP might represent an expression of lung damage and might reflect the respiratory distress consequent to the abnormal inflammation status. Early identification and adequate treatment of COVID-19 patients at high risk for acute respiratory failure are paramount to avoid ARDS and end-organ damage. As reported by Pan et al, chest CT has a pivotal role for the diagnosis and assessment of the severity of lung involvement in COVID-19 pneumonia.[26] Nowadays CT protocols are used to estimate the pulmonary damage [27], and CT findings can be useful to predict adverse outcome [28], but unfortunately CT scan is not available in all the Emergency Departments. Based on our results, we believe that doing LDH and CRP could be useful to the early identification of patients at high risk for acute respiratory failure, even in patients who do not complain dyspnea or affected by slight respiratory failure. These patients could benefit from a prompt hospitalization, a closer observation and correct treatments.

V. CONCLUSION

Elevated LDH and CRP levels could be valuable and favorable prognostic biomarker with high accuracy for predicting the in-hospital mortality in patients with COVID-19. This easily available biomarkers can direct physician worldwide to effectively priority resources for patients at high risk of mortality and to implement more aggressive treatments at an earlier phase to save patients lives.

This study could help healthcare workers to identify those patients at an early stage for early treatment. However, a large sample size and multicenter studies are needed in order to confirm this study.

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