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Research Article

SERUM FERRITIN AND SERUM LACTATE DEHYDROGENASE LEVELS AMONG COVID-19 PATIENTS

ASTHA KAPARUWAN*

Department of Biochemistry, MM Medical College and Hospital, Solan, Himachal Pradesh, India.
***Corresponding author: Astha Kaparuwan; Email: astha.kaparuwan@outlook.com**

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ABSTRACT

Objectives: The aim of this study was to estimate serum ferritin and serum lactate dehydrogenase (LDH) values among COVID-19-positive and COVID-19-negative subjects.

Methods: The study was conducted on 152 cases; 76 were COVID-19 diseased, and 76 were COVID-19 free. Serum ferritin and serum LDH levels were estimated.

Result: Average ferritin levels among COVID-19 diseased were 529.33 ng/ml compared to 450.92 ng/ml among negative individuals. Similarly, the LDH level among positive persons was 338.50 IU/L and 303.30 IU/L among hostile people.

Conclusion: The uncontrolled and dysfunctional immune response is connected with macrophage activation and hyperferritinemic syndrome. Elevated LDH readings seem to reflect that multiple organ injury and failure may play a more prominent role in influencing the clinical outcomes in patients with COVID-19.

Keywords: COVID-19, SARS-CoV-2, Ferritin, LDH, AOSD, Cytokine storm.

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INTRODUCTION

Coronavirus disease (COVID-19) is a transferrable disease produced by the SARS-CoV-2 virus and shows many symptoms affecting various organ systems. Research has given indications regarding the association of an acute inflammatory syndrome linked with COVID-19. The cytokine storm is an uncontrolled and dysfunctional immune response in the immune pathogenic mechanism of COVID-19 [1,2].

Various biomarkers are explored for their role in determining prognosis in patients with COVID-19.

Ferritin, the major intracellular iron storage protein, is an acute phase reactant higher in many inflammatory conditions, including acute infections. Raised values of serum ferritin are the trademark of hyperferritinemia syndromes, a unified term used for macrophage activation syndrome, catastrophic antiphospholipid syndrome, adult-onset still's disease (AOSD), and septic shock. Hyperferritinemia prompted by the disproportionate inflammation due to the infection is linked with admittance to the rigorous care unit and great transience and signifies warning to identify elevated-danger patients to direct the therapeutic interference to control inflammation [3].

Lactate dehydrogenase (LDH) is such a biomarker of significance, exclusively since high LDH levels have been linked to worse consequences during viral infections. Studies have demonstrated serum LDH as a vital marker of vascular permeability in immune-mediated lung injury. Data obtained from COVID-19 people have recommended significant alterations in LDH readings among patients without severe disease [3,4].

Therefore, this study has been formulated for early diagnosis and immediate treatment of the patients to avoid severity.

Aims

- To estimate the level of serum ferritin in COVID-19-positive and negative subjects.
- To estimate the level of serum LDH in COVID-19-positive and negative subjects.
- To correlate serum ferritin and serum LDH in COVID-19-positive and negative subjects.

METHODS

The study was run in the Department of Biochemistry, Shri Mahant Indresh Hospital attached to the Shri Guru Ram Rai Institute of Medical and Health Science, Patelnagar, Dehradun, Uttarakhand, India—the sample size of 152 people, including men and women. Among 152, 76 were COVID-19 positive and 76 were COVID-19 negative cases. Serum ferritin and serum LDH levels were estimated.

Inclusion criteria

- Positive COVID-19 cases were admitted to the COVID ward,
- Aged between 5 and 80 years,
- Healthy subjects as a control.

Exclusion criteria

- COVID-19 recovered cases,
- Pregnant and lactating mother.

Written consent was taken from the subjects included in the study. For COVID-19 patients who were unable, the support was taken from a first-degree relative.

Serum ferritin level was estimated using chemiluminescence immunoassay. Serum LDH levels were assessed using a fully automated VITROUS System 5600 Integrated System. The data obtained were further statistically analyzed.

RESULTS

A total of 152 cases (76 COVID-19 positive and 76 COVID-19 negative) were included in the study (Table 1). COVID-19-negative subjects were considered controls. Serum ferritin and serum LDH levels were estimated.

The ferritin level among COVID-19 positives was 529.33 ng/ml compared to 450.92 ng/ml among negative cases (Tables 2-4). Similarly, the LDH level among positive patients was 338.50 IU/L, and 303.30 IU/L was among negative issues (Tables 2-4).

DISCUSSION

In this study, the mean value of serum ferritin was 772.3 ng/ml. Wu *et al*. found elevated serum ferritin, an independent jeopardy aspect linked with ARDS development [2]. Research by Pastora *et al*. has established that dead cases due to the disease exhibited ferritin levels between 3 and 4 times higher than that found among cured patients after admission, around 1400 ng/mL [5]. Similar AUC for mortality and severity in COVID-19 by Jonathan *et al*. [6]. Various research has supported raising circulating ferritin reading as one of the main modifications during COVID-19 infection [6-9]. Severe COVID-19 patients show high-serum ferritin readings due to cytokine storm and sHLH [10,11]. Plentiful inflammatory cytokines are rapidly produced, including IL-6, TNF-α, IL-1β, IL-12, and IFN-γ, that quicken hepatocytes, Kupffer cells, and macrophages to secrete ferritin during cytokine storm in COVID-19 infection [12,13]. Numerous organ impairments are the result of hyper ferritinemic syndrome and thrombotic storms due to unrestrained and dysfunctional immune responses related to macrophage initiation [14,15]. Notably, serum ferritin also plays a pathogenic part in the progression of inflammation through its bonding with the T-cells and mucin domain 2 (TIM-2) by helping the expression of multiple proinflammatory mediators [5]. Some studies have demonstrated that the H chain of ferritin drives macrophages for inflammatory cytokine production.

Several organ injuries and catastrophes represented added and noticeable roles in disturbing the clinical consequences among COVID-19 cases, which may be due to elevated serum LDH readings. In our study, we observed that the average reading of serum LDH was found to be 666.1IU/L among covid-infected cases. Raised serum LDH among badly affected COVID-19 cases was by various research [16,17]. SARS-CoV-2-affected subjects demonstrated higher LDH in the study by Zhou *et al*. COVID-19 mRNA clearance ratio tremendously allied with serum LDH was mentioned by Yuan *et al*. Serum LDH more than equal to 273 U/L has a higher probability of acquiring ARDS ($p<0.001$, log-rank test) among infected cases. Raised serum LDH related to adverse consequences among COVID-19-infected people was stated by Henry *et al*. [16-18]. Several organ injuries and lessened oxygenation with upregulation of the glycolytic process are the causes of abnormal biochemical changes and readings. The increased H^+ ion concentration due to mounted lactic acid from infection and tissue injury catalyzes the stimulation of enzyme metalloproteases and augments angiogenesis intervened by macrophage [17]. Cytokine-mediated tissue injury and LDH secretion result from acute viral infections [17]. In the meantime, LDH present in lung tissue (isozyme 3) can be likely to enhance the release of LDH as a severe form of interstitial pneumonia, frequently sprouting into severe respiratory distress syndrome (RDS) among COVID-19 infected cases [12].

Table 1: Age distribution

S. No.	Age group (in years)	COVID-19-positive cases (n=76)	COVID-19-positive cases (n=76)
1.	5–20	5	03
2.	21–40	21	24
3.	41–60	35	30
4.	61–80	15	19

Table 2: Ferritin and LDH levels among positive and negative cases

Parameters	COVID-19-positive	COVID-19-negative	Significance
Ferritin	772.3±233.2 ng/ml	671.3±174 ng/ml	p=0.003*
LDH	666.1±27.8 IU/L	583.2±32.6IU/L	p<0.00001*

*The result is significant at $P<0.05$

Table 3: Biochemical parameters among males

Parameters	COVID-19-positive male	COVID-19-negative male
Ferritin	529.33 ng/ml	450.92 ng/ml
LDH	338.50 IU/L	303.30 IU/L

Table 4: Biochemical parameters among females

Parameters	COVID-19-positive female	COVID-19-negative female
Ferritin	242.95 ng/ml	220.37 ng/ml
LDH	327.61 IU/L	279.93 IU/L

CONCLUSION

COVID-19 is an infectious disease caused by the RNA virus called SARS-CoV-2 virus and causes too many symptoms affecting multiple organs of our body. Ferritin is an acute phase reactant found to be elevated in many inflammatory conditions like acute infections. Excess ferritin in plasma is the symbol of hyperferritinemic syndromes. The unrestrained and dysfunctional immune response connected with macrophage, hyperferritinemic syndrome, and thrombotic storm ultimately spreads to compound organs. LDH raised in blood has been allied with lawful consequences of viral infections. Research demonstrated LDH as a probable indicator of vascular permeability in immune-mediated lung injury. Elevation in serum LDH appears to replicate injuries to multiple organs of the body, and catastrophe may show a more protruding role in swaying the clinical results in patients with COVID-19. Severe COVID-19 infections can be expected to state greater amounts of LDH as a form of interstitial pneumonia, resulting in ARDS (acute respiratory distress syndrome). Therefore, estimating serum ferritin and LDH would help assess the severity of the patient and manage it in a timely.

AUTHOR CONTRIBUTIONS

The author made the whole contribution to the study.

CONFLICT OF INTEREST

The author declares that no conflict of interest has been reported.

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