

Lactate Dehydrogenase and Serum Ferritin as Predictors of Respiratory Failure in COVID-19 Patients

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Conflict of interest: Nil

Abstract:

Introduction: The pandemic COVID-19 infection with betacoronavirus-2 requires the identification of a reliable and inexpensive tool to quickly identify patients with a more unfavorable outcome. Many biochemical parameters like lactate dehydrogenase, alanine aminotransferase, aspartate aminotransferase, creatine kinase, serum amyloid-A, and inflammatory markers like interleukin-6, C-reactive proteins, serum ferritin, and D-dimer are raised, which are predicting morbidity and mortality in COVID patients.

Objectives: The aim and objectives of the present study are to evaluate serum ferritin and lactate dehydrogenase values, correlating them with oxygen saturation, and predict the cases that are going into respiratory failure.

Materials & Methods: The present study includes 50 COVID-positive patients confirmed by RTPCR who were admitted to the government general hospital Kurnool during the period of September to November 2020. In these patients, 5 mL blood sample was collected, and serum ferritin and lactate dehydrogenase levels were estimated.

Results: Lactate dehydrogenase and serum ferritin levels showed a negative correlation with oxygen saturation in COVID-19 cases during the study.

Conclusion: Lactate dehydrogenase, a marker of tissue damage, and serum ferritin, an inflammatory marker that causes tissue damage by oxidative stress, may be related to respiratory distress as oxygen saturation is decreasing because of lung injury. Hence, lactate dehydrogenase and serum ferritin can be used as predictors of respiratory failure, and more supportive therapies might be given to avoid a poor prognosis.

Keywords: Lactate Dehydrogenase, Serum Ferritin, RTPCR, COVID-19, Respiratory Failure

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Introduction

As of March 2020, many COVID-19 cases were reported across the world, with Symptoms ranging from mild fever, cough, throat pain, and common cold to respiratory distress, leading to the hospitalization of many patients due to severe inflammatory damage to the lungs [1]. The causative agent for the present global pandemic [SARS-CoV-2] routes from Coronaviridae family. Significant numbers of cases are asymptomatic initially and finally end up in intensive care units due to shortness of breath and decreased oxygen saturation. Complications Include ARDS, renal failure, thromboembolic events, and sepsis leading to mortality. Triage is a must for dealing of COVID-19 cases.

Before the arrival of confirmatory test results for COVID-19, the underlying risk of COVID cases can be predicted from the lab results for the sake of the patient's best outcome. Many biochemical parameters, including interleukin-6, serum ferritin,

D-dimers, C- reactive proteins, lactate dehydrogenase, ALT, AST, and creatine kinase, are elevated in COVID patients. Even though the results of CT scans are highly sensitive and specific in detecting SARS-CoV-2 infection, the TOT [turnaround time] for the CT reports is much longer and costlier when compared to the TOT [turnaround time] for biochemistry lab reports. Moreover, the sensitivity and specificity of biochemical markers for COVID-19 are ranking more or less the same with the CT reports.

Materials and Methods

This is a prospective observational study that included 50 patients [age group between 35 and 60 years] confirmed as COVID-positive by RT-PCR [positive confirmation of the presence of the Corona virus obtained through a real-time reverse transcriptase polymerase chain reaction assay] and got admitted to the government general hospital

Kurnool, during the period from September to November 2020 due to COVID-19 pneumonia.

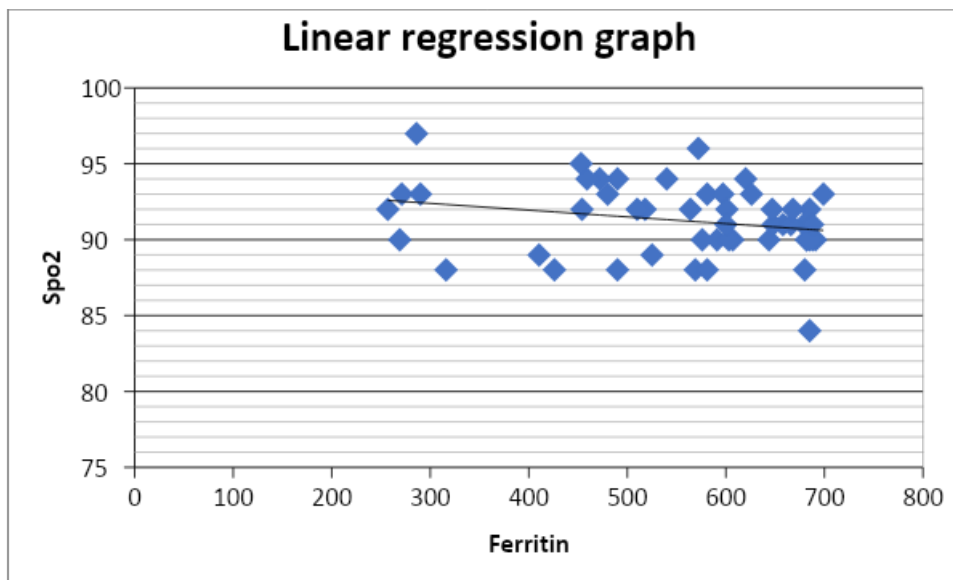
The study was conducted after obtaining approval from the institutional ethical committee. Written informed consent was obtained from each patient who was enrolled in the study. A detailed medical history of the patient was taken from the wards, and the patient's samples were taken for analysis. 5 ml of a non-hemolyzed sample is collected from patients on the 4th or 5th day of the start of symptoms to evaluate serum LDH and serum ferritin levels. The values of LDH are estimated in the semi-auto analyzer by the UV kinetic method, and serum ferritin is estimated by the immuno turbidometric method.

Data of 50 patients entered in an Excel spreadsheet and statistically analyzed by SPSS version 2.1, LDH values were increased in 96% of patients, and serum ferritin was increased in 94% of patients. Correlation analysis between LDH and Spo2 showed an inverse relation ($r = -0.987$, $r^2 = 0.974$, and $p < 0.05$). Correlation analysis between ferritin and spo2 showed an inverse relation ($r = -0.863$, $r^2 = 0.745$, and $p < 0.05$). The ROC curve for LDH showed a cutoff value of 450 IU/L with a sensitivity of 82% and a specificity of 78% in ARDS cases. (AUC) 0.76, $P < 0.05$.

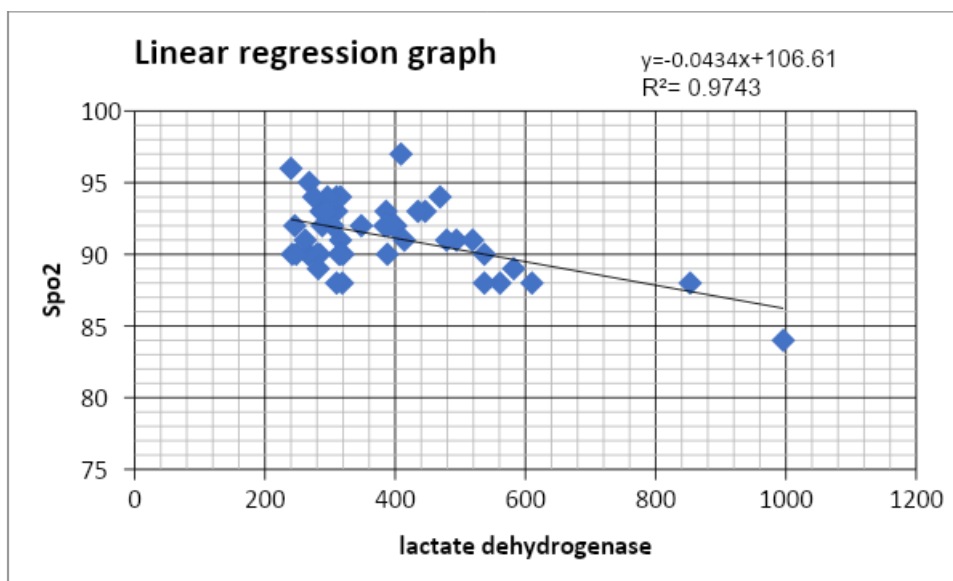
The ferritin cutoff value of 480 ng/mL had a sensitivity of 72% and a specificity of 71% (AUC 0.78, $P < 0.05$).

Results

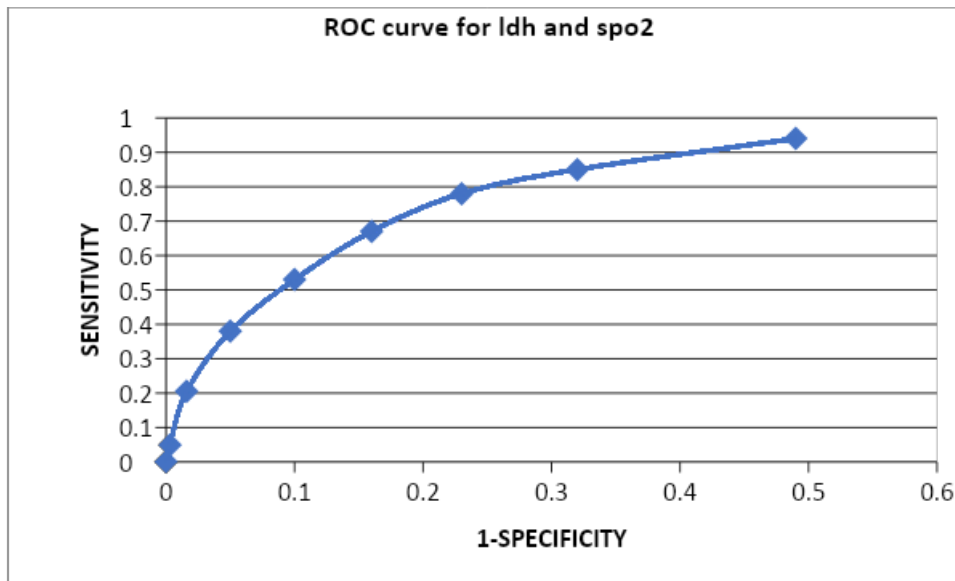
Graphs



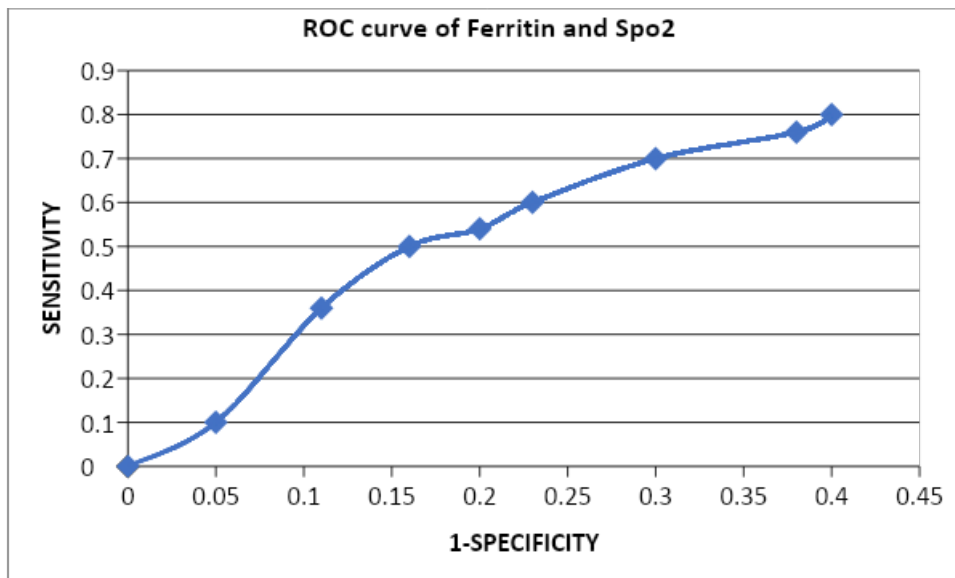
Graph 1: Liner regression graph



Graph 2: Liner regression graph



Graph 3: ROC curve for ldh and SpO₂



Graph 4: ROC curve of Ferritin and SpO₂

Discussion

The clinical spectrum of COVID-19 varies from asymptomatic to interstitial pneumonia, with lung damage leading to ARDS. The existing chest CT severity score [CTSS], even though employed as a semi-quantitative metric for assessing the extent of lung infection and quantifying the disease burden in COVID-19, is not available everywhere, and that is too time-consuming and expensive at this time[2].

In the present study, it was observed that some of the patients admitted to the hospital with dyspnea had high LDH and high serum ferritin values, along with CRP, D-dimer, and other pathological markers, which were obtained early before obtaining the results of the lung US and expensive chest CT. The strongest and most interesting findings of our study were the correlations between

LDH and serum ferritin concentrations with Pao₂/Fio₂ values. LDH is an enzyme utilized in the interconversion of lactate to pyruvate. It is present in almost all the cells, with higher concentrations in the heart, liver, lungs, muscles, kidneys, and RBC.[3] It is an indicator of acute or chronic tissue damage and is hence considered an inflammatory marker.

“Serum ferritin” presents a paradox, as the iron storage protein ferritin is not synthesized in serum yet is to be found there. Serum ferritin is also a well-known inflammatory marker, but it is unclear whether serum ferritin reflects or causes inflammation or whether it is involved in an inflammatory cycle[4] Serum ferritin exists, despite the fact that ferritin is not synthesized in the serum.

Serum ferritin lacks most of the iron it contains when intracellular. The intracellular ferritin must

have 'dumped' its unliganded iron somewhere, where it can participate in Haber-Weiss and Fenton reactions, creating hydroxyl radicals and consequent further cellular damage.[4].

The serum ferritin protein is itself considered benign. Yet the level of serum ferritin correlates with numerous inflammatory and degenerative diseases. Oxidative damage to tissues results in the liberation of free iron into the bloodstream. Ferrous iron liberated is a potent prooxidant. Macrophages and cytokines are involved in the release of serum ferritin from the tissues in COVID cases.

Hyperferritinemia in turn promotes the production of pro-inflammatory (IL- β) and anti-inflammatory cytokines (IL-10). Inflammatory cytokines further cause tissue damage and increase LDH and serum ferritin. Increased lung damage causes respiratory distress with decreased oxygen saturation.

In the present study of COVID-19-positive cases, raised LDH and serum ferritin showed a negative correlation with oxygen saturation in selected cases that landed in acute respiratory distress.

Conclusion

LDH and serum ferritin are negatively related to oxygen saturation and can be used as respiratory failure predictors in COVID-19 cases. They can be used for early identification of patients who require close monitoring and supportive therapies to avoid poor prognosis and respiratory failure

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