Research Article

Role of LDH in Predicating the Severity and Mortality in COVID-19 Patients in Comparison to Other Laboratory Markers at the Time of Admission

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Abstract

Objectives: To correlate Serum LDH levels with severity of COVID 19, and establish LDH as potential marker for COVID 19 prognosis and treatment.

Materials and Method: The study is performed in 204 confirmed COVID 19 cases at a dedicated COVID care Hospital. Lab investigations including Serum LDH, Ferritin, CRP, and D-dimer were estimated at the time of patient admission. The patients were divided into 2 groups namely severe and non-severe based on WHO guidelines. The values for these parameters were compared and the sensitivity and specificity of every parameter was analysed concerning COVID-19 severity and mortality.

Statistical Analysis: Unpaired t-test was used for statistics between the severe and non-severe groups followed by ROC analysis for LDH, CRP, Ferritin, and D-dimer.

Results: The levels of LDH, CRP, and D-dimer were raised in the patients in the severe group as compared to the non-severe group with a significant p-value of < 0.05. Also in ROC analysis the sensitivity and specificity of LDH were found to be good for CRP, Ferritin, and D-dimer. Also, it was observed that among 204 patients, 29 patients died due to COVID, and their serum LDH values were found to be increased which was not the case in the other 3 parameters.

Conclusions: LDH was a better marker in predicting the Severity of COVID-19 disease, also its value is highly significant in predicting the mortality of patients at the time of admission which can help in early prognosis and help in the clinical management of the patient.

Keywords: LDH; COVID 19; Severity

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Introduction

The origin of the novel Corona Virus occurred in the city of Wuhan, China in 2019, and the virus spread worldwide very rapidly. In a month, it transmitted and caused severe respiratory symptoms including acute respiratory syndrome (ARDS) [1]. The virus is RNA beta virus later named SARS-CoV-2 severe acute respiratory syndrome by World Health Organization (WHO) and declared a global pandemic in March 2020 [2]. Since then the disease has affected over 448,313,293 of the world's population and caused more than 6 million deaths [3]. The virus majorly spreads through human-to-human contact or respiratory droplets. The symptoms of the disease vary from mild fever, chills, sore throat, body ache, loss of taste and smell to severe illness such as breathing difficulty, persistent chest pain, and inability to walk or stay awake [4].

The diagnosis of the disease was based on Reverse Transcriptase polymerase chain reaction (RT-PCR) testing and Chest CT to detect the severity of the disease. CT severity score has been used worldwide to assess the severity of the COVID 19 infection, ground-glass opacities are a prominent feature at the early phase of the infection while crazy paving pattern, consolidation and fibrosis is seen in the late phase of the disease [5]. The clinical laboratory has played a major role in the disease diagnosis, prognosis, and treatment of the COVID 19 [6]. There are various laboratory blood investigations that were used for COVID 19 disease treatment along with the Chest CT including Lactate Dehydrogenase (LDH), C - reactive protein (CRP), Ferritin, D- dimer and various cytokines and interleukins such as IL6, IL8, and TNF alpha [6].

Since the last 2 years of the COVID pandemic, there has been a drop of 8% in the death rate due to COVID and it is reported that many cases are not severe and can be treated at an early stage with the correct amount of prognosis and disease management [3].

LDH is an oxidoreductase intracellular enzyme involved in the process of Anaerobic Glycolysis. It facilitates the reversible conversion of Pyruvate to Lactate using NADH as the Co-enzyme [7]. There are 5 types of Isoenzymes of LDH made from 2 types of subunits Muscle (M) and Heart (H). The various forms of LDH isoenzymes are found in different locations of the Human Body, LDH Type 1 is majorly present in Heart tissue, LDH Type 2 in the reticuloendothelial system and RBC'S, LDH type 3 is found in Lungs, LDH type 4 in kidneys and LDH type 5 is present in Liver and

skeletal muscles [5]. The serum levels of LDH are elevated in various conditions such as Haemolysis, sepsis, various other inflammatory conditions for a long time it has been used as a marker for cardiac muscle damage. The increased levels of the enzyme can lead to tissue damage and multiple organ failure and reduced tissue oxygenation. As the LDH isoenzyme 3 is predominantly found in the Lungs the levels of the enzyme are increased, leading to interstitial Pneumonia and ultimately ARDS which is an important symptom of the disease [5]. In this study we hypothesized that LDH is a potential marker that positively correlates with the severity of the COVID 19 disease.

Material and Methods

This is a retrospective study including all the COVID 19 positive patients admitted at the COVID ward of BALCO Medical Centre, unit of Vedanta Medical Research Foundation, Raipur. A total of 204 patients were included from the age group 20 - 78 yrs. (median age 51) from April 2020 to April 2021. The study group included 142 men between the age of 23 – 78yrs. (median age 51) and 65 females within the age of 20- 74 yrs. (median age 51). The patients were tested for COVID 19 by taking Nasopharyngeal and oropharyngeal swabs through RT- PCR Truenat system (closed PCR system). There was a total of 450 patients out of which 205 were selected for the final study, remaining were filtered out due to some incomplete details or were not tested due to some reasons. Among the total number of 204 patients, 29 patients died due to COVID-19 during their hospital stay. The study group was then divided into 2 groups based on the WHO guidelines for Clinical Management of COVID 19, 2021 [8] namely severe and non-severe. The number of patients in the non-severe group was 111 and 95 in the severe group.

All the patients were tested for laboratory parameters which included LDH, CRP, Ferritin, and D-Dimer multiple times during the whole duration of the Hospital Stay.

The biochemical analysis of LDH and CRP was performed in Vitros 250 Dry chemistry analyser by ortho clinical diagnostics and the determination of Ferritin and D-Dimer was performed in Minividas immunoassay system by Biomerieux. In the current study, the data analysis was based on the test values at the time of admission. An unpaired t-test was performed for all the parameters based on the Severity of patients followed by the Receiver's

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Operating Characteristics curve (ROC) curve for the determination of Sensitivity and Specificity of each test parameter in COVID-19 disease.

Results

The statistical analysis was performed using an unpaired t-test and a p-value was calculated to distinguish if the test values were significant to distinguish between the severities of COVID patients. A p-value of < 0.05 was considered to be significant. The ROC curve (Figure 1, ROC curve for LDH shows 79% sensitivity at 95% confidence interval and p value of <0.001) (Figure 2, shows ROC curve for ferritin shows 65% sensitivity at 95% confidence interval with a p value of <0.10) (Figure 3, shows ROC curve for CRP shows 66% sensitivity at 95% confidence interval with p value of <0.001) (Figure 4, shows ROC curve for D Dimer 60% sensitivity at confidence interval of 95% with a p value of <0.005) was plotted for all the parameters for LDH the area under the curve (AUC) was 0.79 with a confidence interval of 95% and a P-value of <0.0001. The AUC value for Ferritin was found to be 0.65 with a confidence interval of 95% and a p-value of 0.10. The AUC value for CRP was found to be 0.66 with a confidence interval of 95% and a p-value of <0.0003. The AUC value for D-Dimer was found to be 0.60 with a confidence interval of 95% and a P-value of < 0.005.
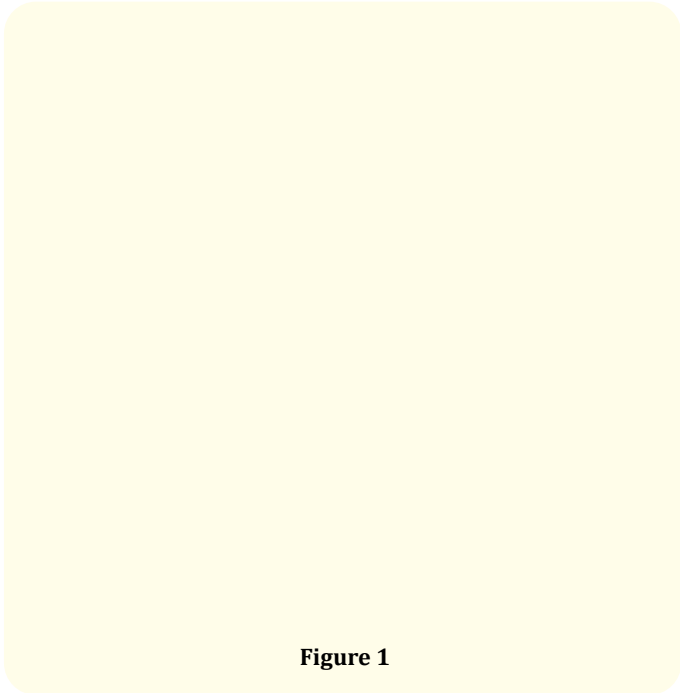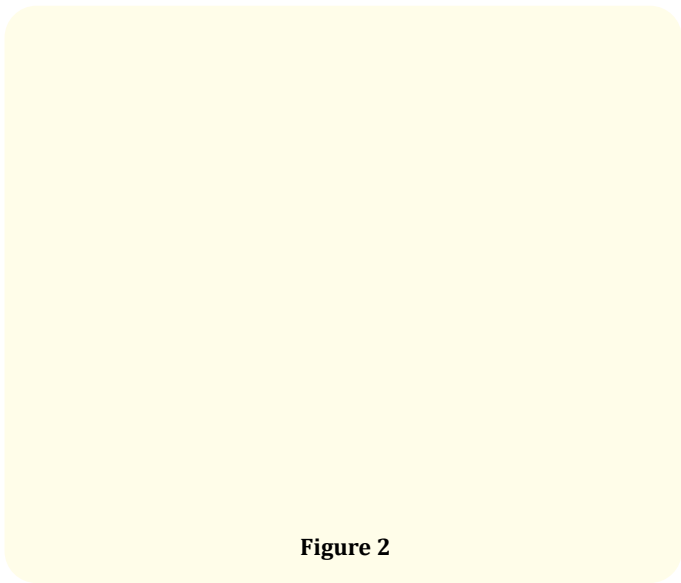

Figure 2

Figure 3

Figure 1

Figure 4

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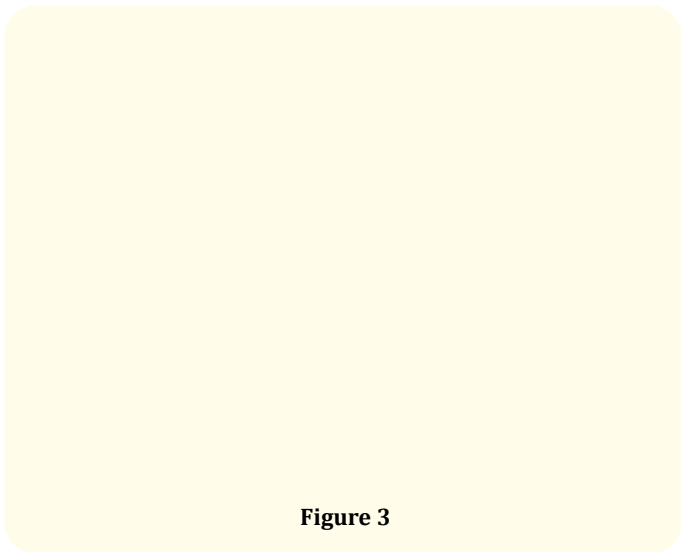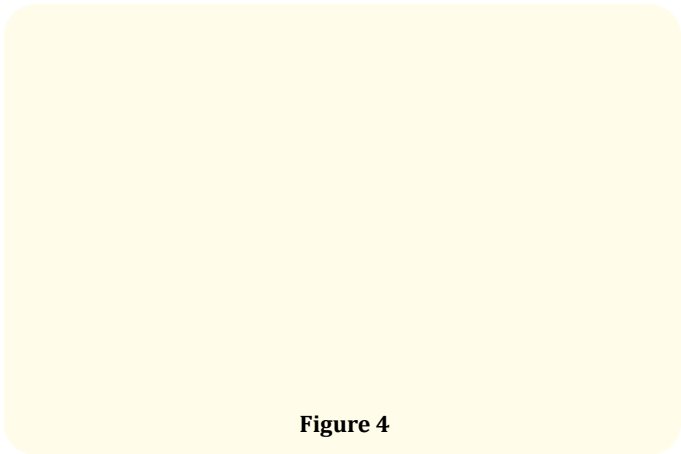
The mean difference between all parameters was calculated concerning the severe and non-severe groups was calculated. The mean difference for LDH was found to be 176.7 ± 23.95. The mean difference for Ferritin was found to be 583.2 ± 360.6. The mean difference for CRP was found to be 14.30 ± 3.881. The mean difference for D-Dimer was found to be 445.1 ± 159.1.

For LDH the patient values were divided into 3 groups according to the test value 1st group consisted of patients with an LDH value of < 200 U/L, 2nd group consisted of patients with an LDH value of <400 U/L and 3rd group consisted of LSH values < 400 U/L. This categorization showed that from all the 29 death patients 28 had LDH values of > 400 U/L.

Discussion

The COVID-19 disease has been reported to cause respiratory symptoms, fever, chills, and various other complications. The severity of disease was found more in the old age patients (> 65 yrs.) as compared to the young aged patients (< 65 yrs.) and also in patients with comorbidities such as hypertension, diabetes, etc. Apart from this, it was observed that most of the patients has mild symptoms and were having good prognosis [9]. To date there is no specific treatment for COVID, precautionary measures are taken focusing on the transmission risk reduction, severity assessment, and early diagnosis [10].

In the past 2 yrs. various studies have been conducted which suggested the significance of laboratory investigations in the treatment and prognosis of COVID-19. The values of Glucose, CRP, Interleukin 6 (IL6), Fibrinogen, Thrombin time, and D-dimer were significantly increased in the severe group compared to the non-severe group [10].

In the current study the t-test's p-value for LDH was found to be significant (<0.05) and ROC value of 0.79 which suggested that LDH has good sensitivity and specificity in predicting the severity of COVID-19. On the other hand, parameters like CRP, D-dimer, and Ferritin had a significant p-value (<0.05) but the ROC analysis suggested that the tests have poor sensitivity and specificity for COVDI-19 severity detection at the time of admission with AUC values of 0.66, 0.60, 0.65 respectively.

The levels of LDH are increased in conditions of inflammation and tissue damage. Severe infections cause cytokine-mediated tissue damage leading to increased blood LDH levels. This suggests that the LDH values are rising with the severity of the infection and thus LDH can be used as a potential marker for the COVID-19 disease severity and mortality prediction.

Conclusion

In the current study we conclude that, despite there are multiple tests like D-Dimer, CRP, Ferritin and different type of Interleukins LDH was found to be a more specific and sensitive marker in predicating the severity and mortality in COVID-19 patients at the time of Admission. Also, it is easily available in most of the laboratories in Indian setup, which makes it a marker of choice.

Conflict of Interest

The authors declare no conflict of Interest.

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