

## Correlation of Lactate Dehydrogenase (LDH) activity, D-Dimer and Severity in a sample of COVID-19 patients in Iraq”

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### Abstract

**Subject:** The coronavirus pandemic, which began in 2019, is a global outbreak of coronavirus disease. The World Health Organization (WHO) also classified Severe Acute Respiratory Syndrome (SARS) as a new coronavirus (SARS-CoV-2). Wuhan, China, was the first place in December 2019 when the pandemic was found. LDH levels were related with a six-fold increase in the risk of developing severe COVID-19 disease.

**Objective of the study :** Estimation of enzyme activity of Lactate Dehydrogenase enzyme (LDH) and d-dimer in patients with COVID-19 to estimate the behavior of enzyme during the period of disease. Correlation of enzyme activity Lactate Dehydrogenase (LDH) with d-dimer. More crucially, elevated LDH was related with a 16-fold increase in the risk of death. Abnormal coagulation function, including elevated D-dimer, has been demonstrated to be more common in deceased patients with COVID-19, and increasing odds of in-hospital death was associated with D-dimer greater than 1 µg/ml. The current study aimed to investigate serum levels of LDH and d-dimer in severity of COVID-19 patients, and to clarify the correlation of these parameters with disease severity

**Material and method :** This study included (48) patients with COVID-19 in severity (confirmed by polymerase chain reaction). COVID-19 patients showed a significant elevation in the levels of all parameters, we concluded a proportional correlation between the aforementioned parameters and COVID-19 suggesting the uses of these tests to the diagnosis of severe cases.

**Results :** This study showed high correlation between activity of lactate dehydrogenase (LDH) and disease progression and severity in patients with COVID-19. Also the study showed high correlation between D-dimer and disease progression and severity in patients with COVID-19.

**Conclusion :** There is correlation between lactate dehydrogenase (LDH) level and D-dimer level in later on during disease Progression. But not and the time of hospitalization.

**Keywords :** COVID-19 , Severe Acute Respiratory Syndrome (SARS) and LDH

## Introduction

Severe Acute Respiratory Syndrome (SARS) was also recognized by the World Health Organization (WHO) as novel coronavirus (SARS-CoV-2). Wuhan, China, was the first location where the epidemic was detected in December 2019. The new disease COVID-19 is only in the early stages of research, and as such, many of the specifics about it are still unclear. This virus spreads easily among people. While symptoms often represent the most infectious state, people may still be infectious for up to two days before showing symptoms (pre-symptomatic transmission). During an average of two weeks, patients with mild disease have been projected to be infectious for two weeks. In more severe cases, they can be infectious for a total of seven to twelve days. While some people appear to be asymptomatic, the virus is known to be transmitted when people are not symptomatic (asymptomatic transmission) (1). Severe infections may result in tissue damage mediated by cytokines and the release of LDH. Due to the fact that LDH is present in lung tissue (isozyme 3), patients with severe COVID-19 infections should expect to have a higher level of LDH in the circulation, as a severe form of interstitial pneumonia(2).

Numerous predictors and therapies being investigated for COVID-19 at the moment are based on experience with the previous coronavirus outbreak, Severe Acute Respiratory Syndrome (SARS), or with other viral respiratory illnesses. Additionally, patients with Middle East Respiratory Syndrome had higher LDH levels (MERS)(3).

COVID-19 increases the level of D-dimer in patients of all ages. Concurrent disease such as diabetes, cancer, or stroke, or a physiological state such as pregnancy, may result in elevated D-dimer levels in COVID-19 patients. On the contrary, the association between elevated D-dimer levels and poor survival highlights the critical nature of detecting D-dimer levels in COVID-19 patients. This test lays the path for enhanced handling of COVID-19. Understanding the mechanism underlying the increase in D-dimer levels in COVID-19 patients may aid in disease management. D-dimer levels may be elevated in these patients as a result of inflammatory responses to viral infections or endothelial cell malfunction, which results in increased thrombin generation. Hypoxia contributes to coagulation disorders through increasing viscosity and the transcription factor-dependent signaling pathway, as well as patient age, underlying diseases, and prolonged hospitalization, all of which increase the patient's chance of developing coagulation disorders. (4,5).

**Patients, Materials and Methods:****Patients:****Patients and study design:**

This is a cross sectional descriptive study that was conducted in Department of chemistry and Biochemistry at the college of Medicine AL-Nahrain University and one hospital (Imamen Al –Kadimain hospital city) on group of 48 patients who need oxygen therapy, patient meets any of the following criteria as determined by the Iraqi Ministry of Health guidelines: appendix C

Respiratory distress (RR > than 30 / m in adults)

Blood oxygen saturation less than 93 % on ambient air.

Lung infiltrates > 50 % of the lung field within 24 hours.

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divided on three sub group. in this group, an estimate was made the parameters (LDH, D-dimer). In addition to other Tests associated with COVID – 19 can be affected. This tests are (C. reactive protein, liver function test, renal function and CBC).

Sub group I: in hospital COVID-19 patients on hospital admission.

Sub group II : In-hospital COVID-19 patients after 10 days from hospital admission VI .

Sub group III : post-hospital COVID-19 patients, one month after the recovery.

**Inclusion criteria:**

Patients who have severity COVID-19

Age of participant above 18 yea

**Exclusion criteria:**

Patients will be excluded from this study is:

Congestive heart failure,

Liver diseases,

Renal failure,

Diabetic mellitus,

Any lung problems, and patients they are taking oral anticoagulants > 6 month.

**Blood sample collection and storage:**

About 5ml of venous blood samples were obtained from patients having severe coronavirus condition. Where the blood is left for 15 minutes at room temperature. After coagulation, serum was separated by centrifugation at 3000 rpm. For 10 min. whole blood was used for performing a complete blood count, and also needed plasma for a D-dimer test using sodium citrate.

Immediate measurements of serum LDH, D- dimer, CRP, creatinine, blood urea, CBC and liver function test were doing using appropriate method.

**Results:**

Non-smoker was the most frequently seen Smoking status ( $n = 99$ , 69%).

For the gender the most frequently observed category was male ( $n = 78$ , 54%).

Frequencies and percentages are presented in Table1-1.

Table1-1 :Show the percentage of gender and smoking frequency in study individuals

Variable	<i>n</i>	%
Smoking		
NO	99	68.75
YES	45	31.25
Gender		
F	66	45.83
M	78	54.17

The means of each time point for LDH are presented in table, indicating significant differences in the median values of LDH1, LDH2, and LDH3. The results of the multiple comparisons indicated significant differences between (LDH1-LDH3) and (LDH2-LDH3) Pairs.

D-Dimer A Friedman rank sum test was conducted to examine whether the medians of D Dimer were equal in the three repeated measurements. the Friedman test was significant  $p < 0.001$ , indicating significant differences in the median values of the D dimer of repeated measurements. significant differences are observed between the: times first - third readings and times second - third readings pairs. Figure 1-2 presents boxplots of D-Dimer1, D-Dimer2, and D-Dimer3. Figure 1-1 presents box and whisker plots of LDH1, LDH2, and LDH3

Table 1-2 : Show the status of LDH and D-Dimer in study individuals

N = 48	time	Median (1st Q-3rd Q)	Mean± SD	Skewness	Kurtosis	SEM
LDH	1st	449.5 (316.75-65)	625.13± 800.43	5.64	35.38	116.75
	2nd	445 (291.00-	484.46± 247.89	1.20	1.00	36.16

		570.25)				
	3rd	267 (223.5-391.5)	326.80± 161.58	1.93	3.82	27.71
D-Dimer	1st	1250 (639.75-2844.5)	2254.56± 2374.6	1.91	3.92	346.37
	2nd	972.5 (528.25-32)	2496.27± 3501.3	2.97	10.29	510.72
	3rd	455 (311.00-630.5)	606.60± 728.96	4.91	26.61	125.02

### (LDH)

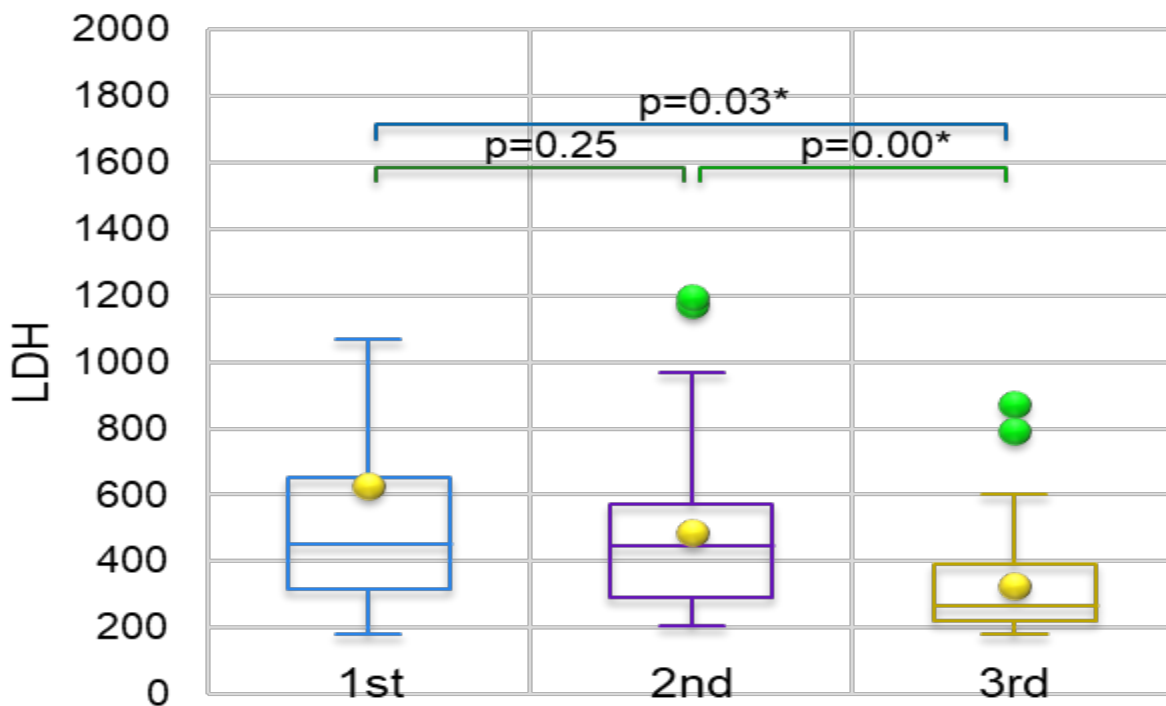


Figure 1-1 Boxplots of LDH in Covid-19 patients in different time points presenting means, Medians, interquartile ranges in addition to minimum and Maximum values

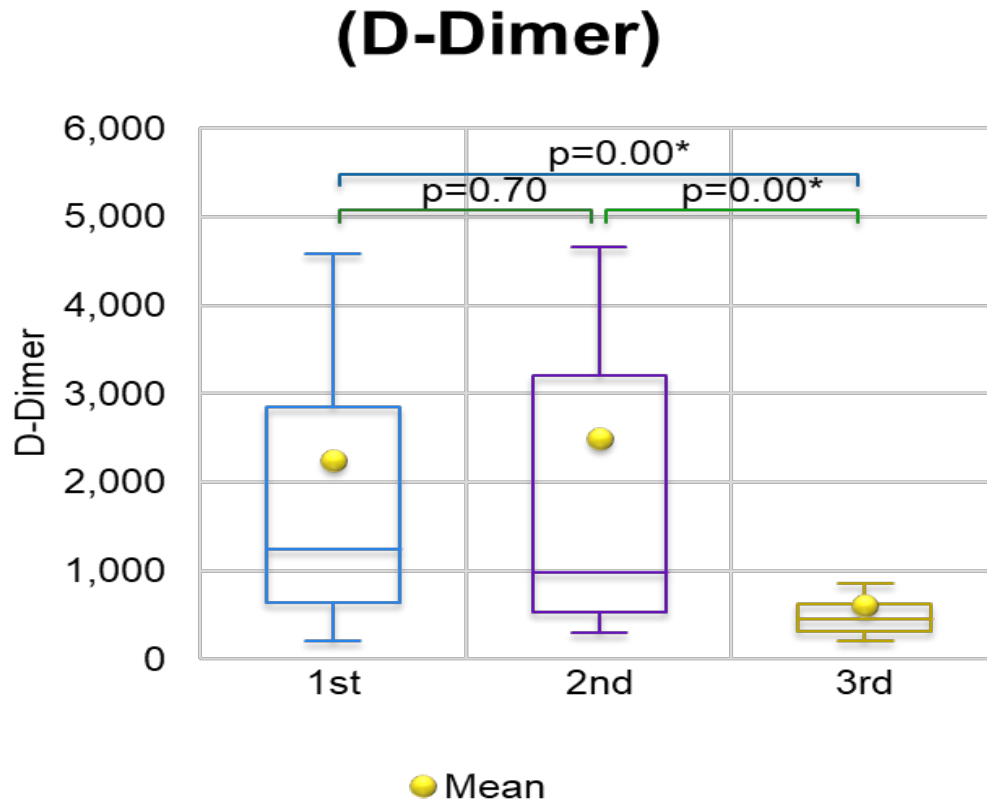


Figure 1-2 Boxplots of D-Dimer in Covid-19 patients in different time points presenting means, Medians, interquartile ranges in addition to minimum and Maximum values.

### Discussion:

A cross sectional study conducted on (48) patients who suffering from severe COVID-19 infection. Three blood samples were taken from each patient at different times and the analyzes required for this study were conducted. In this study, age and gender were taken into consideration as important factors infection with Corona virus, Gender and COVID-19. The present study showed that there are clear statistical differences regarding gender. As the present study showed that men more likely to have sever disease. the percentage of men in this study was 54.17% and the percentage of women 45.1%, this agree with(6) who showed that the rates of injuries and deaths among men are more than among women. Age and COVID-19

This study showed that elderly and those between the ages of (50 – 70)years. The more likely to have sever disease for age had an average of (60.31 ± 12.18). where he was (Min = 35.00, Max = 82, Median = 60 years). this agree with Davies, N.G. et al 2020 (7) who showed an increased number of cases and a greater risk of severe disease with increasing age. Smoking and COVID-19. The present study showed, the percentage of non-smokers

with severe disease was more than the percentage of smokers needing oxygen, as the non-smokers was 68.75% and the patients who smoke were 31.25%. this agree with Lee et al., 2021(8). smoking tended to lower the risk of severe acute respiratory syndrome coronavirus 2. However, these results should be understood with care, and further confirmatory studies are required. Although there are studies indicating the opposite, as studies have shown that smoking can be one of the causes of infection with Covid-19, and that active smokers are more susceptible to Corona virus. as demonstrated in Brake et al., 2020 (9). LDH the present study shows significant difference in LDH concentration which increased in severity of COVID-19 patients were Mean $\pm$  SD (625.13 $\pm$  800.43), (484.46 $\pm$  247.89), (326.80 $\pm$  161.58) respectively and  $p < 0.001$  repeated measurements. this indicates significant differences in the median values of LDH1, LDH2, and LDH3. The results of the multiple comparisons indicated significant differences between (LDH1-LDH3) and (LDH2-LDH3) pair. Where the study indicated in this research that the level of Elevated LDH levels seem to reflect that the multiple organ injury and failure especially the lung, and may play a more prominent role in this pathology in influencing the clinical outcomes in patients with COVID-19, in those who are hospitalized during a period of severe illness. High levels of LDH concentration have contributed to mortality. As seen in Henry et al., 2020 (2).D-dimer the present study shows there is significant differences in the median values of the D dimer concentration which increased in severity of COVID-19 patients were Mean $\pm$  SD (2254.56 $\pm$  2374.6) (2496.27 $\pm$  3501.3) (606.60 $\pm$  728.96) respectively and  $p < 0.001$ , repeated measurements. significant differences are observed between the times first - third readings and times second - third readings pairs. In this study high levels of dimer in hospitalized patients were observed during the period of severe disease. especially in the first days after admission to hospital this agree with Yao et al., 2020( 10). As it was noticed that there was a noticeable increase in the level of D-dimer in patients who were diagnosed with severe disease, as well as deaths in the hospital.

## Conclusion

There is correlation between lactate dehydrogenase (LDH)level and D- dimer level in later on during disease Progression. But not and the time of hospitalization



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