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The impact Lactate dehydrogenase levels enzyme on covid-19 patients

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Abstract
Covid -19 disease in 2020 is considered one of the most dangerous epidemic diseases that afflicted more than a million people in the world, as it quickly turned into delinquent. In this research, we aimed to clarify the clinical relationship of LDH enzyme with this disease. The purpose of this research was that patients who were suffering from a viral infection, lactate dehydrogenase (LDH) were associated with worse results and their condition became very critical, and the relationship between high LDH levels was also examined. Measured at 100 patents in this research, it showed that LDH can be established as a good predictor for early detection of lung infections and serious cases of COVID-19.
Keywords: Lactate dehydrogenase LDH, COVID-19, Coronavirus

Introduction

The outbreak of the novel coronavirus (COVID-19) that is disseminated in 2019 is fast growing and arrived multiple countries in about a month. The cross transmission of covid-19 can result in fatal respiratory disease as severe pneumonia, pulmonary edema and severe acute respiratory distress syndrome (ARDS) **(Wang et al. 2020).**

Lactate dehydrogenase (LDH) is one of the enzymes that involved in the formation of pyruvate from lactate in the most of body tissues cells and elevated after tissues damage (Kolev et al.2008).

There is a greater evidence approving that the level of serum lactate dehydrogenase (LDH) is related to many pathophysiological pathways of diseases, but in pneumonia caused by corona virus the current data related to LDH dynamic alteration has not been well addressed. In the present, the cellular death of many diseases is associated with the presences of LDH in the serum acting as an indicator. and many evidence confirm this. After all, the present information about the corona virus causing the change in LDH level is still missing **(Wu et al. 2020).**

LDH has a molecular weight of 134 kDa, and it made up of four tetramer. The H and M subunit are most common. Five isoenzymes exist, LD1 through to LD5. Although LDH is regarded as an omnipresent enzyme that occurs in each cell's cytoplasm but the structure of its isoenzyme in different tissues is vary. LD1 is primarily Abundant in red blood cells, kidney cells, and heart tissue; and LD5, on the other hand, primarily occurs in hepatocytes and skeletal cells. **Pincus MRet,al 2011.**

AIM OF THE WORK

To improve the medical care service provided to patients suffering from Covid-19 disease.

OBJECTIVES OF THE STUDY

To evaluate the difference between LDH levels that measured in cases of non-severe and severe covid-19 disease.

RESEARCH QUESTION:

What is the difference between the measurement of LDH levels in non-severe and severe covid-19 patients?

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RESEARCH DESIGN AND METHODS

- ✓ **Study Design:**

Case controlstudy will be conducted from 2 April to 20 April2020

- ✓ **Study Setting:**

The study will be conducted at AL-Hakeem Hospital of Najaf city

- ✓ **Target population:**
  The target population will be thepatientssufferingfrom covid-19 at admission or earliest time period of hospitalization.

- **Inclusion Criteria:**
  1) All patients tested positive by PCR for covid-19 and hospitalized at early time period with good o2 saturation from 18 to 65 years.
  2) All patients who tested positive by PCR for covid-19 with severe criteria which is represented as patients with acute respiratory distress syndrome (ARDS) and needing mechanical ventilation, or in intensive care unit (ICU) admission aged from 20to 60 years.

Exclusion Criteria:

1) Patients who refuse to participate in the study.
2) Patients suffered from altered mental status by hypoxia.

Sampling

- **Frame:** patients with covid-19 who fulfilled the inclusion criteria will be enrolled in this study.

- The control group with upper respiratory tract infection URTI and negative covid-19 PCR attending AL-Hakeem Hospital of Najaf city.

- **Method:** simple random sampling

- **Sample Size:** The sample size was calculated and about 100 patients.

- **Data Collection Tools**

There will be 2 groups for assessment, control group with upper respiratory tract infection and PCR test negative for covid-19 at al-hakeem hospital and cases affected by covid-19 and tested positive by PCR at AL-Hakeem Hospital of Najaf city.

The cases tested positive by PCR will be classified to severe and non-severe group (Version 1–6). the medical record system of AL-Hakeem Hospital provide all data concerning socioeconomic information, included patients medical history, concurrent comorbiditiesand the results of chest CT scan.

Lactate dehydrogenase serum level was determined by dry chemistry analyzer (range from 313 to 618 U/L) **(Adams et al.2019).**

- **Data Management:**

The data was collected, coded, and entered into the computer via Excel 2018 program. The data analyzed by using the SPSS program (21) and presented as numbers and percentages using tables and graphs with the CI at 95%.P value <0.05 were used as the limit of statistical significance.

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Ethical Considerations:

- Approval of the responsible authorities was obtained from Kufa University.
- Participant was informed with the aim of the study and its benefit to them as it could help in improving the medical care provided to patients with covod-19.
- Written informed consent was obtained from the participant.
- Ensure the confidentiality of data collected, and that no data were going to be used outside this study without personal approval.
- The researcher's phone number was provided to the participant for any enquiries.
- The participant had the right to withdraw from the research at any time or even refuse to participate from the beginning with no effect on the decisions taken for the plan of the management.
- **BUDGET**
- The budget of the study was offered by the researcher.

Item	**Estimated Costs**
Data Collection	2000D.
Data Management	500 D.
Preparation of final book and presentation	500 D.
Others (Transportation, Printing, Internet access … etc.)	200D.
Total	3200D.

- **TIME TABLE**
- Time needed for preparation of the thesis:

Duration/weeks	**1-3**	**4-6**	**7-8**	**9-10**	**11**	**12**
Protocol Preparation						
Literature review						
Data collection						
Data analysis						
Editing						

Results

The patients enrolled in this study were 100 among them 55 were male and 45 were female (table 1). They had an age range of 20 to 60 years, a median age of 35 years, and 35.6% were over 40 years of age. The patients were divided into 20 severe cases (on-admission) and 30 non-severe. In patients with extreme covid-19 the Concurrent diseases was observed, such as hypertension (12), diabetes (3), and ischemic heart disease (2).

Table.1. basic characteristics of all patients, classification of covid-19 patients by severity.

Baseline characteristics N/value	**N/ Value**
Female	45
Male	55
Urban	60
Rural	30
Age (years, median)35	
Clinical severity	
Non-severe 30	

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Severe	20

Table.2 the underlying condition in severe group

Underlying conditions in	sever group	non sever group
Hypertension	12	4
Diabetes	3	0
Ischemic heart diseases	2	1
Chronic kidney diseases	3	0

LDH level

It is founded that in all patients of covid-19, the LDH level was 430 ± 22 U/. The level of LDH in non-severe patients amounted to 405 ± 27 U/L, the elevated levels of LDH were found in the severe group with a LDH level of 1020 ± 9 U/L ($P < 0.01$).

Discussion

In this study, we focused on the level of LDH in covid-19 patients who are admitted to the AL-Hakeem Hospital of Najaf city (100 patients) for the period between 15 April to 18 June 2020. It is founded that a higher probability of covid-19 disease progression associated with an increase in the level of LDH as 60 U/L with high specificity and**. WU et al. 2020** study revealed that the differenceswas significant in LDH levels between non-severe and severe group of covid-19 ($P < 0.05$) which is consistent with the current study in which there is a statistical significant difference in LDH level and the severity of covid-19 disease.

In glucose metabolism, LDH is a major player which is spread nearly in all tissues and aid in the formation of lactate. When cells damaged this enzyme is released as a result of the destruction of their cytoplasmic membrane **Ding et al 2017.** The importance of LDH as a lung disease marker had noted by previous studies. In a study on Epstein-Barr virus (EBV) infected B cells and uninfected B cells, the researchers found that more LDH transcripts found in infected B cells **Mo, Xiaohui, et al (2018).**Furthermore, in pneumocystis pneumonia (PcP) patientsthe serum levels of LDH elevated, probably was due toinjury of lung **Calderón EJ et al 2010, Huang, et al 2011.**

Traditionally since the 1960s, the marker of cardiac damage used was LDH, but decreased oxygenation and multiple organ injury combined with glycolytic pathway activation can result in abnormal levels. Abnormal level of lactate results in acidic pH in extracellular fluid this high levels caused by infection and tissue injury provoke the metalloproteases activation and intensify angiogenesis which mediated by macrophage **Martinez et al 2011**.The severity of infections may produce tissue damage which mediated by cytokine and LDH release **Martinez et al 2011**. Considering that LDH is found in lung tissue, a severe case of COVID-19 patients can be presented with a high serum level of LDH, as acute respiratory distress syndrome represent the interstitial pneumonia of severe form, which considers the disease hallmark. In any case, various isoenzymes of LDH that contribute to a high level of LDH in COVID-19 has not been determined yet. Furthermore, in thrombotic microangiopathy the LDH levels are elevated, combined with myocardial injury and renal failure **Kaplan et al 2002**, **Patschan, Daniel et al(2006)**, **Zhang, Tao, et al(2014).**In patients with severe COVID-19, the thrombocytopenia and elevation of d-dimer levels have also been reported, these findings propose a hypercoagulable state maybe share in part to mortality and severity of the disease **Lippi et al 2020 and Mario Plebani et al 2020**

The current study revealed that the diseased group with severe covid-19 have the debilitating disease as HTN, DM, CHD which is consistent with Zhao et al. 2020, Who found that the older (50.5 vs. 42.0 years; p=0.049) and with chronic disease (40% vs. 14.8%; p=0.009) have severed case of covid-19 disease compared to mild disease group.

The present study revealed that older age and high level of LDH were reported to be risk factors associated with in-hospital death as mentioned in previous studies by **Wu et al. 2019** who discovered a relationship between older age and severe covid-19 and a higher level of LDH. The current study found that the severity is related to older age which may be due to changes in the immune response between older and younger age as discussed by **Davis et al 2020** who found that those aged under 20 years were half as susceptible to SARS-CoV-2 infection as those aged over 20 years.

Like any study, there are certain limitations to our study. First, the sample size may affect on interpretation of our findings. Larger studies are needed to confirm our results. In addition contributed patients may have received medical intervention as therapy or another type of intervention (mechanical ventilation) which may affect serum LDH levels. At the same time, we propose that to determine the

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prognosis in patients with COVID-19 the LDH value may be utilized as useful and an significant parameter, which may aid in early intervention.

Conclusion

Finally, it may be concluded that elevated level of lactate dehydrogenase enzyme could be used as prognostic marker of severe cases of covid-19 as result LDH of patients must be observed to assess the disease process. These finding need more and larger studies to confirm.

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