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Lactate dehydrogenase level as a COVID-19 biomarker

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Abstract:

Background: Lactate dehydrogenase (LDH) is an intracellular enzyme found in cells in almost all organ systems, which catalyzes the interconversion of pyruvate and lactate, LDH has been proved to be a prognostic factor with high accuracy in diseases involving multiple organ injuries such as acute heart failure (AHF) and severe acute pancreatitis (AP), LDH is a potential prognostic biomarker in patients with COVID-19. **Patients and methods:** This study included 217 non hospitalized patients with confirmed COVID-19 infection in Alexandria, Egypt, these study subjects were randomly selected irrespective of the age group and both genders were included, Assay procedure as manufactory instructions and Reagents of Chema Diagnostics Italy, LDH FL of reagent based on DGKC recommendations. **Results:** The percentage of COVID-19 non hospitalized Patients relation to the serum LDH level, The present study included patients aged from 14 years to 75 years mean age was 44.5 ± 30.5 who were confirmed to have Covid-19 based on real-time reverse transcription-polymerase chain reaction, female gender was more frequent (n=119, 54.8%) than Male gender (n=98, 45.2%). This study reveals high serum LDH levels in 147 patients (67.7%), which was a significant biomarker for COVID-19 diagnosis in non-hospitalized patients (Outpatients and patients under home observation), with a p-value is 0.024 which less than 0.05. **Conclusion and Recommendations:** Serum LDH level is a good biomarker of infection in COVID-19 Outpatients and patients under home observation increased by 67.7%, many other studies revealed LDH is a good marker for COVID-19 hospitalized patients and severe infection.

Keywords: LDH, Lactate dehydrogenase, COVID-19, non-hospitalized patients, biomarker.

1. Introduction:

Lactate dehydrogenase (LDH) is an intracellular enzyme found in cells in almost all organ systems, which catalyzes the interconversion of pyruvate and lactate, with concomitant interconversion of NADH and NAD⁺(¹). The enzyme is composed of two major subunits (i.e., A and B). Lactate dehydrogenase increases in the early stage of myocardial infarction as well as in states of hemolysis. It is most active in the liver, heart, kidneys, striated muscles, lungs, brain, and red blood cells (erythrocytes). In the case of cell damage, lactate dehydrogenase is released from inside them, its concentration and activity in the blood increase(²). Elevated serum LDH is present in numerous clinical conditions, such as hemolysis, cancer, hematologic malignancies, severe infections and sepsis, liver diseases, and many others. Nowadays, there was much evidence suggesting that serum LDH levels serve as a non-specific indicator of cellular death in many diseases(³). LDH has been proved to be a prognostic factor with high accuracy in diseases involving multiple organ injuries such as acute heart failure (AHF) and severe acute pancreatitis (AP)(^{4,5}). LDH is a potential prognostic biomarker in patients with COVID-19(⁶). Elevated LDH signifies tissue hypoperfusion indicates the extent of the disease, hence, may affect prognosis(⁷). Early data Henry et al. reported in COVID-19 patients have suggested significant differences in LDH levels between patients and without the severe disease(⁸). Coronavirus disease 2019 (COVID-19) is a disease that could cause multiple organ injuries including heart(⁹), liver and kidney injuries(¹⁰). There is convincing evidence linking high LDH levels in critically ill patients, through COVID-19, with increasing activity and extent of lung injury(¹¹), however, studies are showing that LDH is not associated with poor prognosis(¹²).

This study aimed to evaluate the prognostic performance of elevated LDH in patients with COVID-19, Outpatients and patients under home observation are included in this study, while hospitalized patients are not included.

2. Patients and methods

2.1. Study population Patients

This study included 217 non hospitalized patients with confirmed COVID-19 infection, these study subjects were randomly selected irrespective of the age group and both genders were included.

It was performed following the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All the studied population was informed about the purpose of sample collection and their consents were obtained. Patients were free to refuse sample collection.

2.2. Data collection

In this cross-sectional study, we obtained data regarding 217 non hospitalized patients with confirmed COVID-19 via real-time reverse transcription-polymerase chain reaction (PCR), they came to Alyamenny laboratory in Alexandria, Egypt for biomarkers and complete blood count investigations, We reviewed the medical records and compiled data between August 12 and December 30, 2020.

2.3. Collection and processing of blood samples:

1 ml blood sample was collected for performing serum Lactate dehydrogenase (LDH) test (Chema Diagnostics Italy, LDH FL of reagent based on DGKC recommendations) on 217 Positive COVID-19 patients for individuals matching in age and gender.

2.4. Assay procedure as manufactory instructions:

Reagents of Chema Diagnostics Italy kit human LDH test and samples allowed to be at room temperature before testing, (serum was separated from a blood

sample by centrifugation), considered normal serum LDH level 225 – 450 U/L.

2.5. Statistical analysis

Data were analyzed using SPSS statistical software, version 20.0(SPSS, Chicago, Illinois, USA). All continuous data are presented as means and standard deviations, while categorical data are presented as numbers and percentages. A chi-square test was used to compare categorical variables. Multivariate regression analysis was performed to analyze relationships between COVID-19 infected patients and serum LDH level, this model was generated using independent variables achieving a p-value of 0.10 during bivariate analysis. Then, the best-fit model was generated without interaction variables. For all

calculations, a p-value of less than 0.05 was considered statistically significant.

3. Results:

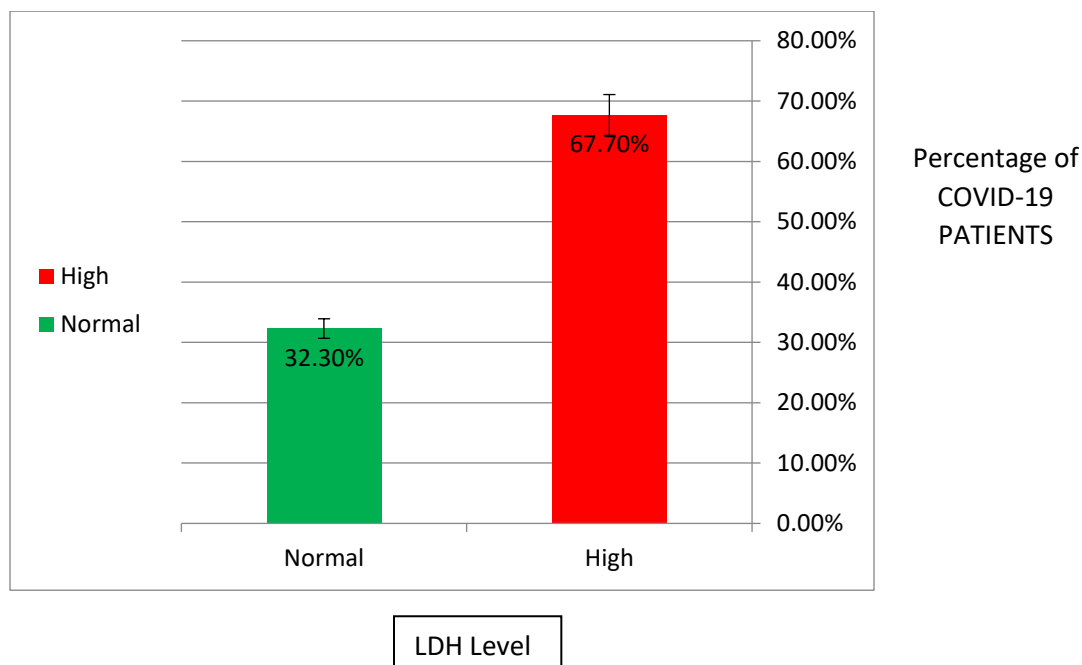
Table (1): shows The percentage of COVID-19 non hospitalized Patients relation to the serum LDH level, The present study included patients aged from 14 years to 75 years mean age was 44.5 ±30.5 who were confirmed to have Covid-19 based on real-time reverse transcription-polymerase chain reaction, female gender was more frequent (n=119, 54.8%) than Male gender (n=98, 45.2%). This study reveals high serum LDH levels in 147 patients (67.7%), which was a significant biomarker for COVID-19 diagnosis in non-hospitalized patients (Outpatients and patients under home observation), with a p-value is 0.024 which less than 0.05.

Table (1): The percentage of COVID-19 non-hospitalized Patients and serum LDH level.

COVID-19 POSITIVE Patients	Serum LDH level				Total	
	*Normal		**High level			
	No.	%	No.	%	No.	%
Male	42	60	56	38.1	98	45.2
Female	28	40	91	61.9	119	54.8
Total	70		147		217	

The chi-square statistic is 9.1871. The p-value is .002437. Significant at $p < .05$.
 The chi-square statistic with Yates correction is 8.3239. The p-value is .003913. Significant at $p < .05$.

Figure (1): Serum LDH level with the percentage of COVID-19 PATIENTS



4. Discussion:

COVID-19 is an emerging viral illness that has rapidly transmitted throughout the world. It has shown that the disease could induce symptoms including fever, dry cough, dyspnea, and fatigue in infected patients^(9,13), COVID-19 is an infectious viral disease, usually accompanied by local or systemic inflammation which may even lead to multiple organ injury. , studies of the association between objective disease status and the laboratory findings may produce more interesting findings⁽¹⁴⁾, Increased ferritin levels could cause a cytokine storm by exerting direct immunosuppressive and pro-inflammatory effects, It has been reported that fatal outcomes by COVID-19 are accompanied by cytokine storm syndrome and ferritin level was significant in COVID-19 home observation patients⁽¹⁵⁾, Severe infections may cause cytokine-mediated tissue damage and LDH release⁽¹⁶⁾. Since LDH is present in lung tissue (isozyme 3), patients with severe COVID-19 infections can be expected to release greater amounts of LDH in the

circulation, often evolving into acute respiratory distress syndrome, For this reason, there was an urgent need to verify and update dynamic variables including LDH as the number of COVID-19 pneumonia accumulates. In the present study, serum LDH was validated for its potential usefulness as a marker for evaluating COVID-19 infection, in 217 Outpatients with mild symptoms and patients under home observation were included in this study, with confirmed COVID-19 infection, it showed elevation of serum LDH level in 147 patients from 217 with a percentage of 67.7 % which has a p-value of 0.024, It was a significant value. The present study included patients aged from 14 years to 75 years mean age was 44.5 ±30.5 who were confirmed to have Covid-19 based on real-time reverse transcription-polymerase chain reaction (PCR). The elevation of serum LDH level has been associated with pulmonary disorders such as interstitial lung disease, chronic obstructive pulmonary disease, pulmonary embolism, and microbial pulmonary

disease, and pleural fluid LDH has been used to determine pulmonary cell injury and inflammation⁽¹⁷⁾, Published studies have reported that 40% of COVID-19 patients present with elevated LDH, which has been associated with a higher risk of ARDS and death⁽¹⁸⁾. Chan et al., 2020 reported increasing of LDH level in 3 cases from a familial cluster, 6 cases more than 60 years⁽¹⁹⁾, Chen et al., 2020a reported that increase of LDH level in 20 patients from 29 (15 milds, 9 severe, 5 critical cases)⁽²⁰⁾, Huang et al., 2020 reported LDH level increased in all 13 ICU cases⁽⁶⁾, Wu et al., 2020 reported increasing LDH level in ARDS 201 cases⁽²¹⁾, Li et al., 2020a (meta-analysis) 1994 cases reported increasing LDH level in 28% of cases⁽²²⁾, Li et al., 2020b from a study on 54 cases they reported increasing of LDH level in most cases⁽²³⁾, Liu et al., 2020 reported that LDH level increased in all 12 cases studied⁽²⁴⁾, Mo et al., 2020 reported increasing of LDH level in 85 severe cases and not increased in 70 mild cases⁽²⁵⁾,

Conflict of interest

There are no conflicts of interest.

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