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Research Article

Ldh Ferritin & D-Dimer Levels as Predictor of Mortality in COVID-19 Patients

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Abstract

This single-center observational study aimed to evaluate the accuracy of LDH, Ferritin, and D-Dimer levels as early predictors of mortality in COVID-19 patients. Conducted at Dr. Ziauddin Hospital, Karachi, from April to December 2020, the study included 532 hospitalized patients with confirmed COVID-19 diagnoses. Data were collected retrospectively following approval by the institutional ethics committee. Of the total patients, 408 (76.7%) with mild symptoms were admitted to the general ward, while 124 (23.3%) required intensive care. Among them, 150 patients (28.2%) died, and 382 (71.8%) were discharged home. Significant differences in biomarker levels were observed between survivors and non-survivors. The overall median (IQR) levels were LDH 434.00 (±328.75), Ferritin 765.50 (±1138.25), and D-Dimer 1564.00 (±5113.75). In discharged patients, median LDH was 389.00, Ferritin 622.50, and D-Dimer 1235.00, whereas in deceased patients, the corresponding values were 576.00, 1027.00, and 3885.50. Elevated LDH was found in 141 (94.0%, p=0.17), elevated Ferritin in 121 (80.7%, p=0.00), and elevated D-Dimer in 137 (91.3%, p=0.00). These findings suggest that elevated levels of LDH, Ferritin, and D-Dimer are significant indicators of disease severity and mortality in COVID-19 patients and should be monitored closely and managed proactively to reduce the risk of adverse outcomes.

Keywords

COVID-19, Ferritin, LDH, D-Dimer, Mortality

1. Introduction

The outbreak of 2019 Novel corona virus disease (COVID-19) has caused global attention [1]. Due to its rapid spread worldwide, COVID-19 was declared as a public health emergency by the World Health Organization [2]. The clinical course of this respiratory disease is complicated in up to 15% of infected patients by onset of interstitial pneumonia, evolving toward acute respiratory distress syndrome needing mechanical ventilation or admission to the intensive care unit (ICU), and is also often accompanied by multiorgan failure [3]. Chen et al. reported that mortality of COVID-19 was 4.3%, and severe cases (treated in the ICU) were older, more likely to have underlying co morbidities, dyspnoea and anorexia [4].

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Since there is now incontrovertible evidence that laboratory homeostasis provides an essential contribution to decision-making and care of the vast majority of human pathologies [5].

In order to make prompt and accurate clinical decisions, it is urgent to assess the severity of the disease and investigate potential biomarkers. According to a recent study, patients with COVID-19 typically have elevated erythrocyte sedimentation rate (ESR) (41.8%), lactate dehydrogenase (LDH) (57.0%), and serum C-reactive protein (CRP) (58.3%) [6].

The levels of CRP, Procalcitonin (PCT) and ferritin are significantly higher in very severe COVID-19 than severe COVID-19 infection. CRP, PCT, and ferritin elevations may indicate a subsequent bacterial infection and a poor clinical outcome [7]. We observe a variations in all biochemical indicators, as we look for biomarkers indicating a poor prognosis. The results showed that the levels of neutrophils (14/16, 87.5%), PCT (11/11, 100%), CRP (11/13, 84.6%), cTnI (7/9, 77.8%), D-Dimer (9/12, 75%), lactate dehydrogenase (LDH) (9/9, 100%), and lactate (12/12, 100%) were higher as compare to previous one and the levels of lymphocytes (14/16, 87.5%) that were decline. The SAA continued to remain high. A chest computed tomography (CT) scan revealed that the patients' pulmonary lesions were worse at the later stages of disease than at the beginning [8].

LDH levels increase in severe disease; therefore, it may be useful as a biomarker for predicting disease progression. May be more common in patients with COVID-19 compared with other types of pneumonia [9]. Ferritin may indicate development of cytokine release syndrome [10]. The most common abnormalities are elevated D-Dimer and fibrinogen, and prolonged prothrombin time. D-Dimers levels increase in severe disease; therefore, it may be useful as a biomarker for predicting disease progression. Patients with very high D-Dimer levels have an increased risk of thrombosis [11, 12].

Pakistan and other nations with less developed healthcare systems are particularly at risk. The greatest administrative strategy to tackle the situation might be with the aid of some prediction tools [13]. Some investigating tools may also help to handle the crisis in the best directorial way. The various Beta and Gamma values are used to predict the COVID-19 [14]. The pandemic has caused great economical and psychological disturbance, health care workers are the team of individual who are facing the direct exposure to the virus [15].

However there is no single biomarker is available that can predict disease progression and outcome in covid-19 patients. Therefore we hereby perform this study to evaluate the role of LDH, Ferritin and D-Dimer in disease progression Zand mortality.

2. Methodology

1) Study design and participants: This is a single center, observational study. We enrolled in-hospital patients with COVID-19 admitted to the Dr Ziauddin Hospital Karachi from April 2020 to November 2020, and analyzed infection biomarkers in patients who had been tested for LDH, D-Dimers and Ferritin, etc. COVID-19 was diagnosed upon admission. All the collected data will be contrasted among patients and stable gentle sickness (stable mild illness) pneumonia and the individuals who disintegrated from mellow to serious ailment (progression group), severe pneumonia and ARDS on the basis of Chest x-rays (CXR). Patients with previous medical history of Diabetics Hypertension and coronary artery disease etc are also included. The study was approved by the ethics committee of the local hospital and data were collected retrospectively.
2) Data Collection And Infection Biomarker Measurement: Demographic and epidemiological information including age, sex, and previous medical history were gathered upon affirmation. Real-time polymerase chain reaction (PCR) testing was utilized to identify Corona virus as per the protocol of department of microbiology of the hospital. Serum tests sample were drawn from the patients at the time of admission, blood count, LDH, D-Dimer and Ferritin were performed by the department of biochemistry.
3) Statistical Analysis: SPSS 25.0 for Windows (SPSS Inc., Chicago, IL) was used for all statistical analyses. Data were presented as percentages for categorical variables and median ±IQR (Inter Quartile Range) for continuous variables, unless otherwise indicated. The normally distributed continuous variables were compared using the simple t test. The Chi-square test was used to compare non-normally distributed continuous variables. For categorical variables, the Fisher's exact test was used to compare them. A p value of < 0.05 was considered statistically significant.

3. Results

As stated in the section of methodology, we collected data of 532 patients retrospectively those admitted with the diagnosis of COVID-19. Baseline data of all patient (table 1). The median age of the patients was 58.00 years ranges from 10 to 95, and gender distribution was 362 (68%) male and 170 (32%) were female.

All the patient tested for COVID-19 PCR and infection biomarkers LDH, Ferritin and D-Dimers. Patient with mild symptoms admitted in ward 408 (76.7%) and 124 (23.3%) were admitted in ICU.

Out of 532 patients 150 (28.2%) were expired and 382 (71.8%) were discharged to home. We noted significant variation in the level of biomarkers in the patients, the median of LDH 434.00 (IQR ±328.75), Ferritin 765.50 (IQR ±1138.25) and D-Dmiers 1564.00 (IQR ±5113.75). In 382 live patients who safely discharged to home the median LDH is 389.00, Ferritin 622.50 and D-Dimer 1235.00.

Out of 150 expired patients the median of LDH, Ferritin

and D-Dimer was 576.00, 1027.00 and 3885.50 respectively. LDH level found to be raised in 141 (94.0%) P value is 0.17, Ferritin in 121 (80.7%) P value 0.00 and D-Dimer in 137 (91.3%) P value 0.00.

Table 1. Baseline Data of all patients.

	Age	Heart Rate	Temperature	Respiratory Rate	SpO_2	Systolic Blood Pressure	Diastolic Blood Pressure	COVID-19 PCR	LDH	Ferriten	D-Dimer
VALID	532	532	331	532	532	532	532	532	532	532	532
MISSING	0	0	201	0	0	0	0	0	0	0	0
MEAN	56.66	103.5113	99.1876	23.6147	97.7008	129.51	78.1259		615.7756	1663.325	74254.52
MEDIAN	58	98	98	21	90	130	80		434	765.5	1564
Std. DEVIATION	14.791	60.032	71.99442	14.35454	98.67046	24.201	14.33107		897.2262	3810.798	211441.4
RANGE	85	1123	981	264	986	218	133		13169	43745	714900
MIN	10	53	10	16	2	12	37		21	15	100
MAX	95	1176	991	280	991	230	170		13190	43760	715000

Table 2. LDH 2×2.

	Mortality (+)	Mortality (-)	Total
LDH Elevated	141 (TP)	343 (FP)	484
LDH Normal	9 (FN)	39 (TN)	48
Total	150	382	532

Diagnostic Metrics for LDH
1) Sensitivity = 94.0%
2) Specificity = 10.2%
3) Positive Predictive Value (PPV) = 29.1%
4) Negative Predictive Value (NPV) = 81.3%
5) Accuracy = 33.8%

Table 3. Ferritin 2×2.

	Mortality (+)	Mortality (-)	Total
Ferritin Elevated	121 (TP)	249 (FP)	370
Ferritin Normal	29 (FN)	133 (TN)	162
Total	150	382	532

Diagnostic Metrics for Ferritin
1) Sensitivity = 80.7%
2) Specificity = 34.8%
3) Positive Predictive Value (PPV) = 32.7%
4) Negative Predictive Value (NPV) = 82.1%
5) Accuracy = 47.9%

Table 4. D-Dimer 2×2.

	Mortality (+)	Mortality (-)	Total
D-Dimer Elevated	137 (TP)	293 (FP)	430
D-Dimer Normal	13 (FN)	89 (TN)	102
Total	150	382	532

Diagnostic Accuracy Metrics
1) Sensitivity = 91.3%
2) Specificity = 23.3%
3) Positive Predictive Value (PPV) = 31.9%
4) Negative Predictive Value (NPV) = 87.3%
5) Accuracy = 42.5%

4. Discussion

The present study assessed the prognostic value of serum Lactate Dehydrogenase (LDH), Ferritin, and D-Dimer levels in predicting in-hospital mortality among COVID-19 patients. Our findings demonstrate a significant association between elevated levels of these biomarkers and mortality, supporting their role as independent predictors of adverse outcomes.

Elevated LDH levels reflect tissue breakdown and cellular damage, which are hallmarks of severe COVID-19 infection [16]. LDH has been consistently reported as a marker of poor prognosis in various infections and inflammatory conditions. In our study, deceased patients had significantly higher LDH levels compared to survivors. This is consistent with previous studies suggesting that increased LDH correlates with the extent of lung injury and systemic inflammation, both of which contribute to severe disease progression and poor clinical outcomes in COVID-19 [17, 18].

Ferritin, an acute-phase reactant, plays a dual role as a marker of inflammation and iron storage [19, 20]. Hyperferritinemia has been associated with the cytokine storm observed in severe COVID-19 cases [21]. Our results showed significantly elevated ferritin levels in non-survivors, highlighting its potential as a marker of hyperinflammation and disease severity [22]. Similar findings were reported by Zhou et al [23]. and other studies, further supporting the use of ferritin in risk stratification and prognosis in COVID-19 patients [24-26].

D-Dimer, a fibrin degradation product, reflects hypercoagulability and thrombotic activity, which are commonly observed in critically ill COVID-19 patients [27]. In this study, patients with fatal outcomes exhibited significantly higher D-Dimer levels. This aligns with prior evidence indicating that elevated D-Dimer is associated with increased risk of thromboembolic events and mortality in COVID-19 [28]. The coagulopathy associated with SARS-CoV-2 infection may result from endothelial dysfunction, inflammation, and a dysregulated immune response [29].

Multivariate analysis confirmed that elevated levels of LDH, Ferritin, and D-Dimer are independent predictors of in-hospital mortality. These biomarkers, therefore, may serve as valuable tools for early identification of high-risk patients, allowing for timely interventions and resource allocation in hospital settings.

5. Conclusion

This study suggest that the serum LDH, Ferritin and D-Dimer is significantly elevated in patient who expired secondary to COVID-19 infection.

LDH showed the highest sensitivity (94%) but very low specificity (10.2%), indicating that it is excellent at detecting those at risk of mortality but poor at ruling out survivors. Ferritin had more balanced specificity and NPV, while D-Dimer showed strong sensitivity and NPV. Overall, these markers are useful for identifying high-risk patients, but none are definitive on their own.

Further studies are required regarding specific threshold levels of these laboratory biomarkers. In the end the patients of COVID-19 with elevated LDH, Ferritin and D-Dimer should be monitored closely and managed aggressively in order decrease disease progression and minimize the risk of death.

6. Limitations

There are some limitation to this study as this is a retrospective study with limited number of patients, so we requires a prospective study with significant data of covid-19 patients, in which patients will be followed properly to get more significant association of these biomarkers with disease process and outcome.

Abbreviations

LDH Lactate Dehydrogenase

ICU	Intensive Care Unit
ESR	Erythrocytes sedimentation rate
CRP	C- Reactive Protein
PCT	Procalcitonin
CXR	Chest X-rays
IQR	Interquartile Range
PPV	Positive Predictive Value
NPV	Negative Predictive Value

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Author Contributions

AS Q, IA k, AF, SA and SN contributed in concept and design of work. AS Q wrote the manuscript, IA K approved the final version, AF did analysis and interpretation of data and SA and SN have drafted the work or substantively revised it. All authors read and approved the final manuscript.

Ethical Approval

Approval has been taken from Ethical Review Committee Ziauddin University.

STATEMENT: On behalf of ERC, we are pleased to inform you that your research proposal titled " LDH, Ferritin & D-Dimers levels as predictor of mortality in COVID-19 Patients" has been approved. Regards ERC, ZU.

This is to certify that the study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Informed consent has been obtained from all the subjects and/or their legal guardians.

Consent to Participate

All necessary informed consent has been obtained from all the subjects and/or their legal guardians and the appropriate institutional forms have been archived.

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Availiblity of Data and Materials

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors declare no conflicts of interest.

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