Relationship between serum lactate dehydrogenase levels and prognosis in patients infected with omicron and delta variants of COVID-19: A cross-sectional study

Fatemeh Ostadi [a,1], Babak Choobi Anzali [b,*,2], Hamid Reza Mehryar [b,2]

[a] Department of medicine, School of medicine, Urmia University of Medical Sciences, Urmia, Iran
[b] Emergency Medicine, Department of emergency Medicine, School of Medicine, Urmia University of Medical Sciences, Urmia, Iran

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ABSTRACT

Determining the prognosis of COVID-19 is crucial for understanding disease trends and developing effective treatment strategies, particularly for severe cases. However, there is currently insufficient evidence regarding the role of lactate dehydrogenase (LDH) in COVID-19 and its prognostic implications. This retrospective cross-sectional study analyzed data from all patients hospitalized at Urmia Imam Khomeini Hospital between September 2021 and March 2023 with a diagnosis of COVID-19 involving the Delta and Omicron variants. Patient information, including age, sex, duration of hospitalization, admission to the intensive care unit (ICU), strain type, and outcomes, was extracted. Exclusion criteria encompassed myocardial infarction, lung, liver, blood, skeletal muscle diseases, injury, neoplasm, pancreatitis, pregnancy, poisoning, unwillingness to participate in the study, and the use of ascorbic acid. A total of 609 patients with an average age of 54.80 years were included in this study. Among these patients, 56.3% were female, and the mortality rate was 20.7%. The serum LDH levels were significantly higher in patients who succumbed to the disease (P < 0.001), those requiring ICU admission (P < 0.001), and female patients (P = 0.02) compared to other groups. Furthermore, the LDH serum levels exhibited a strong significant correlation with the duration of hospitalization (r = −0.11, P = 0.007). The results revealed that there is a difference in the mean serum LDH levels between deceased patients and discharged patients (P < 0.001). The findings indicate that elevated serum LDH levels are associated with increased mortality, prolonged hospitalization, ICU admission, and infection with the Delta variant of COVID-19.

1. Introduction

The COVID-19 pandemic caused by the novel coronavirus SARS-CoV-2 has had a significant impact on global health, with millions of reported cases and a substantial number of deaths worldwide [1]. The emergence of new variants of the virus, such as the Omicron and Delta variants, has raised concerns about their potential impact on disease severity and prognosis [2]. Understanding the prognostic factors that contribute to the clinical outcomes of COVID-19 patients is crucial for effective patient management and resource allocation [3].

Lactate dehydrogenase (LDH) is an enzyme involved in the conversion of lactate to pyruvate, playing a vital role in cellular metabolism [4]. LDH is present in various tissues and is released into the bloodstream in response to cellular damage or injury. Elevated levels of LDH have been associated with tissue damage, inflammation, and poor prognosis in various diseases, including respiratory infections [5].

While several studies have investigated the association between LDH levels and disease severity in COVID-19 patients, limited evidence exists regarding the specific relationship between LDH serum levels and prognosis in individuals infected with the Omicron and Delta variants [6,7]. Omicron and Delta are of particular interest due to their increased transmissibility and potential for higher disease severity compared to earlier strains [8].

Therefore, this study aims to evaluate the relationship between LDH serum levels and prognosis in patients infected with the Omicron and Delta variants of COVID-19. By examining LDH as a potential prognostic

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* Corresponding author.
  E-mail address: anzalibabak@yahoo.com (B.C. Anzali).
[1] Address: Nursing and Midwifery Faculty, Campus Nazlu, 11 KM Road Seru, Urmia, West Azerbaijan, IRAN. Postal Code: 575611–5111. Fax: +984412752378
[2] Address: Medicine Faculty, Campus Nazlu, 11 KM Road Seru, Urmia, West Azerbaijan, IRAN. Postal Code: 575611–5111. Fax: +984412754921

marker, we aim to contribute to the understanding of disease progression and identify potential indicators for risk stratification and targeted therapeutic interventions.

The findings of this study have the potential to provide valuable insights into the clinical course and outcomes of COVID-19 patients infected with the Omicron and Delta variants. Such knowledge can aid healthcare professionals in predicting disease severity, optimizing treatment strategies, and allocating resources effectively to ensure the best possible outcomes for patients.

1.1. Study design

This study was designed and conducted as a retrospective cross-sectional analysis. Data pertaining to all patients hospitalized with a diagnosis of COVID-19 involving the Delta and Omicron variants at Imam Khomeini Hospital in Urmia between September 2021 and March 2022 were extracted.

1.2. Participants

A purposive convenient sampling technique was used to select participants for this study. Exclusion criteria encompassed a history of myocardial infarction, lung, liver, blood, skeletal muscle diseases, injury, neoplasm, pancreatitis, pregnancy, poisoning, unwillingness to participate in the study, and the use of ascorbic acid. Patients with cognitive impairments or language barriers that would hinder their ability to participate effectively were excluded from the study.

1.3. Sample size

Based on the available patient population, a total of 609 participants were included in this study (Fig. 1). Considering the confidence interval of 95% and the power of 80% in the study by Li et al. [9], the minimum sample size was calculated to be 580 using G*Power 3.1 [10]. Regarding the attrition rate of 5%, the final sample size was considered to be 609 participants. Our work has been reported in line with the STROCSS criteria [11].

$$n = \frac{z_{1-\alpha/2}^2 \times p(1-p)}{d^2}$$

1.4. Data collection

Data collection for this study was carried out by accessing the files of patients admitted to Imam Khomeini Hospital in Urmia. The research team retrieved relevant information from the medical records of all patients diagnosed with COVID-19 and infected with the Delta and Omicron variants during the specified period. The data collected from the files included demographic details such as age and gender, clinical parameters such as duration of hospitalization and ICU admission, strain type, and patient outcomes. Strict adherence to patient confidentiality and ethical guidelines was maintained throughout the data collection process to ensure the privacy and anonymity of the individuals involved. By gathering information from patient files, a comprehensive dataset was compiled, enabling a robust analysis of the relationship between serum lactate dehydrogenase levels and prognosis in patients infected with the Omicron and Delta variants of COVID-19.

This study adhered to ethical guidelines and obtained ethical approval from the relevant research ethics committee. Confidentiality and anonymity of the participants' data were strictly ensured, and data was used solely for research purposes.

1.5. Data analysis

The data were examined, and descriptive statistics such as mean, standard deviation, relative frequency, and percentage were used. To investigate the relationship between serum LDH levels and other variables, appropriate statistical tests such as independent t-test, chi-square test, and Pearson correlation test were employed. The significance level in this study was set at less than 0.05.

Furthermore, to control for other influential variables, multivariable analyses such as analysis of variance (ANOVA) and multiple regression models were used. The results were analyzed using P-values and
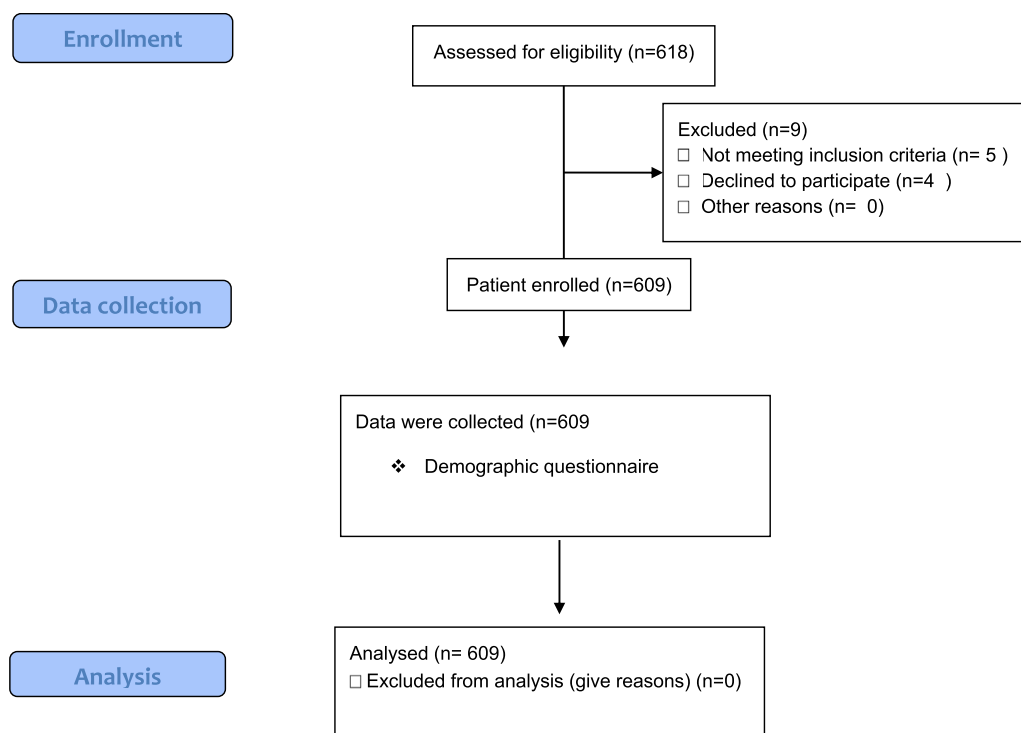

Fig. 1. Flow diagram of entering subjects in the study.

appropriate statistical software.

The findings of this study have the potential to elucidate the relationship between serum lactate dehydrogenase levels and prognosis in patients infected with the Omicron and Delta variants of COVID-19.

2. Findings

A total of 609 patients with a mean age of 54.80 years were included in this study. Out of the total sample size, 43.7% were male (266 participants) and 56.3% were female (343 participants). Among the participants, 46% (280 individuals) were infected with the Omicron variant, while 54% (329 individuals) were infected with the Delta variant. The majority of participants, 83.7% (510 individuals), were married, while 16.3% (99 individuals) were single. In terms of residential status, 69.4% (423 individuals) lived in urban areas, while 30.6% (186 individuals) resided in rural areas. Among the participants, 38.5% (235 individuals) were smokers, while 61.5% (374 individuals) were non-smokers. In terms of income, 53.3% (325 individuals) reported having not enough income, 32.1% (196 individuals) reported having enough income, and 14.6% (88 individuals) reported having more than enough income (Table 1).

Results showed for the Omicron variant, the LDH level is 212.90 $\pm$ 597.07, indicating a mean LDH level of 212.90 with a standard deviation of 597.07. Similarly, for the Delta variant, the LDH level is 330.47 $\pm$ 726.17, with a mean LDH level of 330.47 and a standard deviation of 726.17. the results revealed that there is a significant difference in serum LDH levels between patients infected with the Omicron and Delta variants of COVID-19 ($P < 0.001$). Patients with the Delta variant generally exhibit higher LDH levels compared to those with the Omicron variant. The LDH levels presented in the table provide insights into the biochemical characteristics of the two variant groups and their potential implications for disease severity and prognosis (Table 2).

The LDH levels in the serum are presented as the mean value $\pm$ the standard deviation (SD) in Table 3. For deceased patients, the mean LDH level is 320.50 $\pm$ 1004.16. The results revealed that there is a difference in the mean serum LDH levels between deceased patients and discharged patients ($P < 0.001$).

Based on the Table 4, it can be concluded that the LDH levels are significantly higher in patients hospitalized in the ICU ward compared to those in the non-ICU ward. The mean LDH levels in the ICU ward (354.34) are considerably higher than in the non-ICU ward (202.02) ($P < 0.001$). This suggests that patients in the ICU may be experiencing more tissue damage or medical conditions associated with elevated LDH levels.

When considering gender differences, it was observed that female patients had significantly higher LDH levels compared to male patients ($P = 0.02$) (Table 5). Correlation analysis showed a strong significant

Table 1
Demographic characteristics of the study participants.

Variables		Number	Percent
Gender	Male	266	43.7
	Female	343	56.3
Variants of COVID-19	Omicron	280	46
	Delta	329	54
Marital status	Married	510	83.7
	Single	99	16.3
Residential status	Urban	423	69.4
	Rural	186	30.6
Smoking	Yes	235	38.5
	No	374	61.5
Income level	Not enough	325	53.3
	Enough	196	32.1
	More than enough	88	14.6
Age		Mean	SD
		54.80	15.52

SD=Standard deviation

Table 2
The mean score of the treatment adherence in the study.

Dimensions	Mean	SD
Treatment adherence to HD	238.37	67.78
Medication adherence	85.33	39.45
Fluid restrictions	127.75	29.26
Diet recommendations	99.93	45.22
Total treatment *adherence*	551.38	181.71

Table 3
Comparison of mean LDH serum levels in deceased and discharged patients.

Patients	Serum LDH level SD $\pm$ Mean	Minimum	Maximum	P-Value
Deceased	1004.16 $\pm$ 320.50	662	1108	P[a]< 0.001
Discharged	578.81 $\pm$ 204.04	275	1846	
Total	666.81 $\pm$ 289.59	275	1846	

[a] Independent T-test

Table 4
Comparison of mean LDH serum levels in patients hospitalized in general and ICU wards.

Wards	Serum LDH level SD $\pm$ Mean	Minimum	Maximum	P-Value
General	$\pm$579.95 202.02	275	1108	P[a]<0.001
ICU	894.83$\pm$354.34	398	1846	
Total	666.81$\pm$289.59	275	1846	

[a] Independent T-test

Table 5
Comparison of mean LDH serum levels in patients with COVID- 19 by gender.

Gender	Serum LDH level SD $\pm$ Mean	Minimum	Maximum	P-Value
Male	636.26 $\pm$ 229.71	662	1108	P[a]= 0.02
Female	690.51 $\pm$ 326.97	275	1846	
Total	666.81 $\pm$ 289.59	275	1846	

[a] Independent T-test

association between LDH serum levels and age ($r = -0.11$, $p = 0.007$) (Fig. 2). However, it is important to note that the clinical implications of this gender difference require further investigation.

Correlation analysis showed a strong significant association between LDH serum levels and the duration of hospitalization ($r = -0.11$, $p = 0.007$) (Fig. 3). This finding suggests that higher LDH levels are associated with longer hospital stays in COVID-19 patients.

Interestingly, no significant difference in LDH serum levels was observed between vaccinated and non-vaccinated patients ($P = 0.62$) (Table 6). This finding suggests that vaccination status may not directly impact LDH levels in individuals infected with the Omicron and Delta variants of COVID-19.

3. Discussion

The present study aimed to investigate the relationship between serum lactate dehydrogenase (LDH) levels and prognosis in patients infected with the Omicron and Delta variants of COVID-19. The findings provide valuable insights into the potential role of LDH as a prognostic marker and its association with disease severity, mortality, hospitalization duration, ICU admission, and gender differences.

The results of this study demonstrated that elevated LDH serum levels were significantly associated with increased mortality in COVID-19 patients infected with the Omicron and Delta variants. Patients who succumbed to the disease had higher LDH levels compared to those who were discharged. This finding suggests that LDH could serve as a useful prognostic indicator for identifying individuals at higher risk of poor
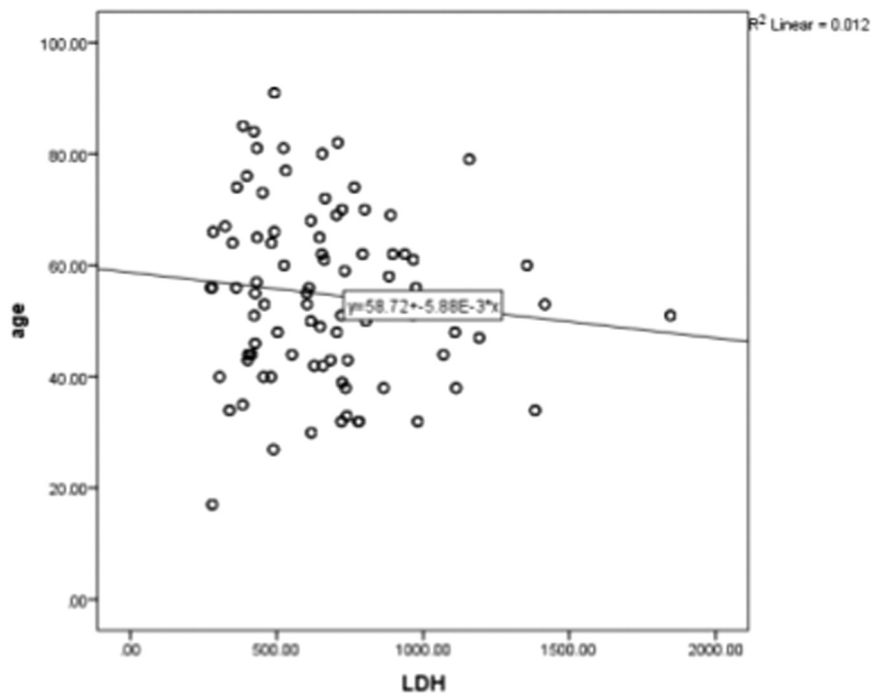
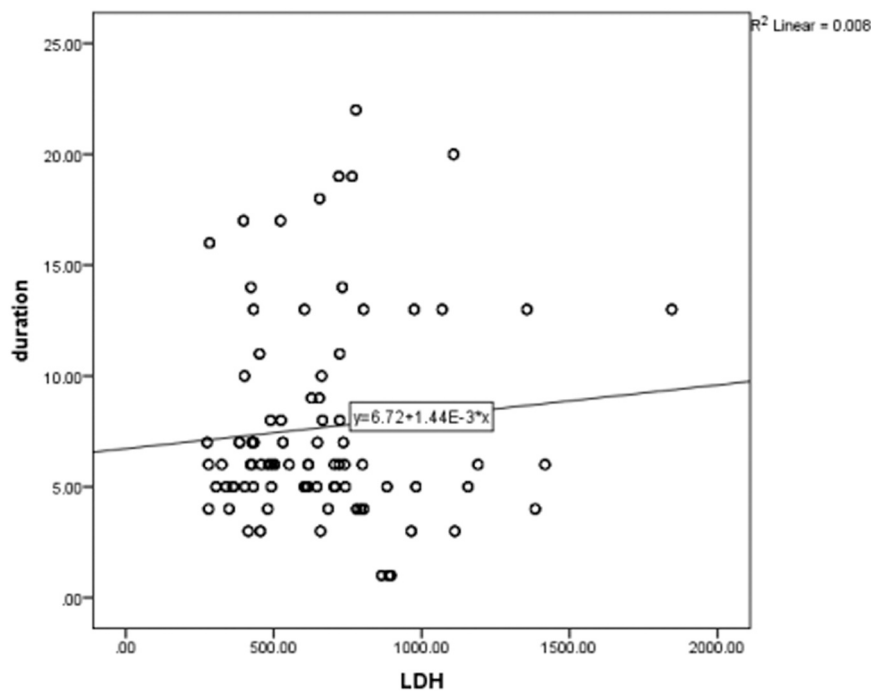**Fig. 2.** Pearson correlation coefficient between age and LDH.

Fig. 3. Pearson correlation coefficient between age and the duration of hospitalization.

Table 6

Comparison of mean LDH serum levels in vaccinated and unvaccinated patients with COVID- 19.

Patients	Serum LDH level Mean ± SD	Minimum	Maximum	P-Value
Vaccinated	670.98 ± 302.41	280	1846	P[a]= 0.62
Unvaccinated	658.90 ± 264.03	275	1417	
Total	666.81 ± 289.59	275	1846	

[a] Independent T-test

outcomes.

Furthermore, the study revealed a significant correlation between LDH levels and the duration of hospitalization. Patients with higher LDH levels tended to have a prolonged hospital stay, indicating a potential link between LDH and disease progression. This association highlights the importance of LDH as a marker of disease severity and the need for close monitoring and appropriate management strategies for individuals with elevated LDH levels.

Another important finding of this study was the association between LDH levels and ICU admission. Patients who required ICU care exhibited

significantly higher LDH levels compared to those who did not. This suggests that LDH may reflect the extent of tissue damage and the severity of the disease, as ICU admission is often an indicator of critical illness. Monitoring LDH levels could aid in identifying patients who are more likely to require intensive care and may help in resource allocation and treatment decision-making [12].

Interestingly, the study also observed gender differences in LDH levels, with female patients demonstrating higher LDH levels compared to males. This finding raises the possibility of gender-specific variations in disease pathogenesis and immune response.

It is worth noting that there was no significant difference in LDH levels between vaccinated and non-vaccinated patients in this study. This suggests that LDH may reflect disease severity and prognosis independent of vaccination status. However, it is important to consider that the study was conducted during a specific time period, and the impact of vaccination on LDH levels may vary over time and with the emergence of new variants.

The findings of this study contribute to the growing body of evidence on the prognostic significance of LDH in COVID-19. LDH is an enzyme involved in cellular metabolism and is released into the bloodstream in response to tissue damage or injury [13]. Elevated LDH levels have been associated with poor prognosis in various diseases, including respiratory infections. The current study adds to this knowledge by specifically examining the relationship between LDH and the Omicron and Delta variants, which are of particular concern due to their increased transmissibility and potential for higher disease severity [14].

Severe infections can lead to tissue damage and the release of LDH through cytokine-mediated mechanisms [15]. In the case of severe COVID-19 infections, patients with interstitial pneumonia progressing to acute respiratory distress syndrome often release higher amounts of LDH into the bloodstream. LDH, specifically isozyme 3 found in lung tissue, is implicated in this process. However, the specific contribution of different LDH isoenzymes to the observed LDH elevation in COVID-19 remains unknown. Moreover, LDH levels are also increased in thrombotic microangiopathy, which is associated with renal failure and myocardial injury [16–18]. Reports have indicated elevated levels of D-dimer and thrombocytopenia in severe COVID-19 patients, suggesting that a hypercoagulable state may contribute to the severity of illness and mortality [19,20].

Several studies have identified LDH as a predictor of worse outcomes in hospitalized patients [5,21]. Many of the prognostic factors and treatment approaches being investigated for COVID-19 are based on experiences with the previous coronavirus outbreak, severe acute respiratory syndrome (SARS), and other viral respiratory infections. LDH levels were also found to be elevated in patients with Middle East Respiratory Syndrome (MERS) [22]. The elevated LDH levels may indicate that multiple organ injury and failure play a significant role in influencing clinical outcomes in patients with COVID-19.

However, several limitations should be considered when interpreting the findings of this study. First, the study design was retrospective and cross-sectional, which limits the ability to establish causality and determine the temporal relationship between LDH levels and prognosis. Prospective longitudinal studies are needed to validate these findings and assess the dynamic changes in LDH levels over the course of the disease.

Second, the study was conducted at a single center, which may introduce bias and limit the generalizability of the results. Multi-center studies involving larger and more diverse patient populations are warranted to confirm the findings and enhance their external validity.

Third, the study did not investigate the underlying mechanisms linking LDH levels to disease severity and prognosis. Future research should focus on elucidating the biological processes and pathways through which LDH contributes to COVID-19 pathogenesis and clinical outcomes.

4. Conclusion

In conclusion, the present study highlights the significant association between serum LDH levels and prognosis in patients infected with the Omicron and Delta variants of COVID-19. Elevated LDH levels were found to be associated with increased mortality, prolonged hospitalization, ICU admission, and gender differences. These findings support the utility of LDH as a potential prognostic marker and emphasize its role in predicting disease severity and optimizing treatment strategies. Further research is needed to validate these findings and explore the underlying mechanisms involved in LDH-related pathophysiology in COVID-19.

CRediT authorship contribution statement

Fatemeh Ostadi; **Babak Choobi Anzali**: Study concept, data collection, writing the paper and making the revision of the manuscript following the reviewer's instructions. **Hamid Reza Mehryar**: Study concept, reviewing and validating the manuscript's credibility.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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