International Journal of Advanced Smart Convergence Vol.11 No.4 260-265 (2022)
http://dx.doi.org/10.7236/IJASC.2022.11.4.260

IJASC 22-4-29

Analysis of Lactate Dehydrogenase Levels of COVID-19 Patients in a Korean Hospital According to Sex and Age

[1#]Sun Gyu Kim [2#]Hee Seung Song, [3*]Jae Kyung Kim

[1] *Department of Medical Laser, Dankook University Graduate School of Medicine, Cheonan, Republic of Korea*
[2] *Department of Nursing, Sangji University, Wonju, Republic of Korea*
[3] *Department of Biomedical Laboratory Science, Dankook University, Cheonan, Republic of Korea*
gpmc5683@medical.or.kr, nerowolf@naver.com, sky6115@sangji.ac.kr

Abstract

This study aimed to determine whether lactate dehydrogenase (LDH) levels in coronavirus disease (COVID-19) patients in Korea were higher than those in patients without COVID-19, and the effect of sex and age on LDH levels. A retrospective, observational study was conducted to measure LDH levels in 247 and 225 female and male COVID-19 patients, respectively, who were admitted to the study hospital between April 1 and October 30, 2020. Serum LDH levels were measured using an automated analyzer. Results: LDH levels were elevated in both male and female patients with COVID-19. Among patients with COVID-19, LDH levels were higher in males than in females, and LDH levels were higher in patients with COVID-19 than in patients in the control group. In the analysis of differences in LDH levels by age, LDH levels in patients with COVID-19 increased statistically significantly with age in males and females (males: p=0.001, females: p=0.001). By examining the differences in LDH levels according to sex and age, this study contributed to the basic biochemical data available in Korea, particularly regarding patients with COVID-19. Further research may be needed to examine confounding variables.

Keywords: *SARS-CoV-2, COVID-19, Lactate Dehydrogenase, Laboratory Tests*

1. INTRODUCTION

Coronavirus disease (COVID-19) is a respiratory infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a virus belonging to the coronavirus family and the Sarbecovirus subgenus of Betacoronaviruses [1]. As of November 15, 2022, 631,935,687 COVID-19 cases and 6,558,850 related deaths worldwide had been reported to the World Health Organization [2]. In Korea, the first patient was reported on January 20, 2020, and by November 15, 2022, a total of 26,290,754 confirmed cases and 29,748 deaths had been reported [3]. The highly contagious SARS-CoV-2 Delta variant emerged in early 2021 and spread globally [4]. More than 80% of patients with COVID-19 present with a mild form of the disease, approximately 15% require inpatient treatment with oxygen therapy, and 4–5% progress to severe disease requiring mechanical ventilation [5]. The increase in confirmed cases of COVID-19 and deaths has created a burden of

Manuscript Received: November. 27, 2022 / Revised: December. 2, 2022 / Accepted: December. 3, 2022
Corresponding Author: nerowolf@naver.com
Tel: +82-41-550-1451, Fax: +82-41-559-7934
Professor, Department of Biomedical Laboratory Science, Dankook University, Korea

15% require inpatient treatment with oxygen therapy, and 4–5% progress to severe disease requiring mechanical ventilation [5]. The increase in confirmed cases of COVID-19 and deaths has created a burden of large medical expenses, and has been recognized as a serious public health problem. In hospitalized patients with COVID-19, blood tests provide information on the progression, prognosis, and response to treatment [6]. Moreover, early identification is important in improving the prognosis of patients with COVID-19 [7].

2. THEORY

Previous studies have evaluated the accuracy and ease of use of lymphocyte counts and lactate dehydrogenase (LDH) levels, and the importance of laboratory tests, including interleukin 6, C-reactive protein (CRP), D-dimer, and ferritin in evaluating patients with COVID-19 [8]. LDH is a major enzyme in the body that catalyzes the reversible oxidation reaction of lactic acid and pyruvic acid. It is distributed in most tissues, including the heart, liver, muscles, lungs, kidneys, and blood [9]. LDH is an inflammatory marker and common indicator of acute or chronic tissue damage [10]. A meta-analysis suggested the usefulness of LDH in identifying COVID-19 [11]. In addition, it was reported that sex was a risk factor contributing to the severity of the disease, and that age was a factor that had a significant effect on mortality. However, there is a lack of studies examining LDH increases and the differences by age and sex in Koreans with COVID-19. This study aimed to examine these differences and understand the related hematological and biochemical characteristics.

3. EXPERIMENTS

3.1 Methods

This study compared LDH levels according to age and sex in patients with and without COVID-19 admitted to xxxxx Hospital, from April 1 to October 30, 2020. A control group was created from patients who underwent medical checkups at xxxxx University Hospital. This study was approved by the Clinical Research Review Committee of xxxxx University (Institutional Review Board xxx, 2020-12-010).

3.2 Lactate Dehydrogenase Test

Serum LDH levels of patients with COVID-19 were measured using an automated analyzer (TBA-2000FR, Canon Medical Systems Corporation, Japan). LDH levels were evaluated by the diagnostic testing department at the xxxxx Hospital according to standard blood-testing procedures.

3.3 Statistical Analysis

Categorical data were reported as frequencies and percentages. Analyses of LDH levels according to sex and age were performed using independent sample t-tests and one-way ANOVA. All statistical analyses were conducted using SPSS ver.19.0 (IBM Corp, Armonk, NY, USA), and statistical significance was defined as $p<0.05$.

4. RESULTS

4.1 Characteristics of Patients with COVID-19 and Controls

From April to October 2020, a total of 472 patients with COVID-19 (247 females and 225 males) were

admitted to xxxxx Hospital. The average age of the women and men was 64.6 years and 60.2 years, respectively. Additionally, a total of 120 femmale and male patients without COVID-19 (47 females and 73 males) were included in the control group, with an average age of 49.8 years and 52.0 years, respectively (Table 1).

Table 1. Characteristics of Patients with COVID-19 and Control Patients

Variable	Patients with COVID-19 (N=472) n (%)	Control patients (N=120) n (%)
Sex		
Male	225 (47.7)	73 (60.8)
Female	247 (52.3)	47 (39.2)
Age (years)		
0–29	35 (7.4)	6 (5.0)
30–59	139 (29.4)	80 (66.7)
≥60	298 (63.1)	34 (28.3)

4.2 Differences in Lactate Dehydrogenase Levels According to Sex

The overall mean LDH level of patients with COVID-19 patients was 502.5 ± 212.5 IU/L and was significantly higher in male patients than in female patients (p=0.006). In the control group, the mean LDH level was 198.6 ± 34.6 IU/L and was similarly higher in male patients than in female patients, although the difference was not statistically significant (p=0.104). Moreover, the LDH levels were higher in patients with COVID-19 than in patients in the control group (Table 2).

Table 2. Lactate Levels (IU/L) of Patients with COVID-19 and Control Patients According to Sex

	All patients	Female patients	Male patients	P
Normal controls (n=120)	198.6 ± 34.6	192.6 ± 27.8	202.5 ± 38.0	0.104
COVID-19[b] patients (n=472)	502.5 ± 212.5	484.8 ± 186.8	521.9 ± 236.3	0.006

Values are presented as mean ± standard deviation.

4.3 Differences in Lactate Dehydrogenase Levels According to Age

Participants were classified into three age groups: 0–29 years, 30–59 years, and ≥60 years. LDH levels by age are shown in Table 3. In the control group, no statistically significant differences were noted between the LDH levels according to the age group (p=0.140). However, LDH levels differed significantly by age in patients with COVID-19 (p=0.001). In addition, although the LDH levels did not differ significantly by age in the control group, they increased with age in female patients (p=0.202), but decreased with age in male patients (p=0.198). In contrast, LDH levels increased significantly with age in both male and female patients with COVID-19 (male: p=0.001, female: p=0.001) (Table 3).

Table 3. LDH Llevels (IU/L) of Patients with COVID-19 and Control Patients According to Age

			0–29 years	30–59 years	≥60 years	P
Normal (n=120)	controls	All patients	185.3 ± 15.1	199.4 ± 37.8	198.9 ± 28.7	0.140
		Female patients	179.8 ± 7.5	190.6 ± 28.7	205.1 ± 28.4	0.202
		Male patients	213.0	204.9 ± 41.7	196.8 ± 38.0	0.198
COVID-19 (n=472)	patients	All patients	405.9 ± 25.6	452.3 ± 11.7	537.2 ± 13.8	0.001
		Female patients	386.6 ± 118.9	445.7 ± 140.2	511.1 ± 204.5	0.001
		Male patients	425.3 ± 171.0	454.0 ± 141.3	587.7 ± 335.0	0.001

Values are presented as mean ± standard deviation.

5. DISCUSSION

In this study, the LDH level of COVID-19 patients was significantly higher in males than in females. These results were similar to the findings of a clinical study on COVID-19 pneumonia conducted in 2020 in Wuhan, China [12]. Increased LDH levels in COVID-19 patients may indicate necrosis or lung damage, which increases the likelihood of developing pneumonia as a complication of COVID-19 [13]. High LDH levels have been reported to be significantly higher in patients who die than in patients who survive, and have also been associated with poor prognosis and need for ICU treatment [11]. In addition, males may be at a greater risk than females of developing critical disease or suffering from fatal conditions, which may have a significant impact on their prognoses, particularly in patients with comorbidities such as high blood pressure, diabetes mellitus, and cardiovascular disease [14]. In addition, the level of serum LDH by sex may be used as an index to rapidly assess the severity of COVID-19 [15]. In males, higher LDH levels may indicate a higher susceptibility to COVID-19 than in females, and LDH may be useful as an indicator of disease severity in males [12]. Although this study did not compare disease severity by sex, our results confirmed that among patients with COVID-19, males had higher LDH levels than females, and patients with COVID-19 had higher LDH levels than patients in the control group.

In the analysis of differences in LDH levels by age, the LDH levels of COVID-19 patients increased statistically significantly with age in both males and females. In contrast, in the control group, the LDH levels increased with age in female patients and decreased with age in male patients. In patients with COVID-19, the risk of death increases sharply with age, with 116 deaths per 1,000 individuals in patients aged ≥75 years [16]. On the other hand, another study found that age was not an independent risk factor for disease severity [15]. Due to these discrepancies, cumulative research results are needed.

This study had several limitations. First, controlling for confounding variables, such as the underlying disease of the patients in the control group and comorbidities in patients with COVID-19, was not possible, which may have affected our ability to determine the differences in LDH levels according to sex and age. Second, the exact mechanism for elevated LDH levels in patients with COVID-19 was not identified. Lastly, as this was a retrospective study, its analysis contained a limited number of previously obtained results. Nonetheless, the finding that LDH levels were higher in patients with COVID-19 than in non-infected individuals is useful.

6. CONCLUSION

LDH levels were high in both males and female patients with COVID-19, and showed a more marked increase with age in male patients than in female patients. In addition to previous studies, the results of this study suggest that LDH test values should be confirmed in COVID-19 diagnosis and progress confirmation for domestic patients.

Further studies are needed to determine LDH levels controlling for confounding variables, such as underlying diseases, and to compare LDH levels according to smoking status, chronic disease status, and clinical symptoms of patients with COVID-19 in Korea.

Blood test results of COVID-19 positive inpatients provide information on treatment progress, prognosis, and response. By confirming the difference in LDH levels between Korean COVID-19 patients and non-infected patients according to gender and age, it contributed to the accumulation of basic hematological and biochemical data in Korea.

REFERENCES

[1] T. Singhal. "A review of coronavirus disease-2019 (COVID-19)," *Indian Journal of Pediatrics*, Vol. 87, pp. 281-286, 2020.
DOI: https://doi.org/10.1007/s12098-020-03263-6

[2] World Health Organization. Worldwide, status of COVID-19, 15 Nov 2022, https://covid19.who.int.

[3] Ministry of Health and Welfare. Korea, Domestic status of COVID-19, 15 Nov 2022, https://ncov.kdca.go.kr/?brdId=1&brdGubun=11&ncv

[4] W. Yang, J. Shaman, "COVID-19 pandemic dynamics in India and impact of the SARS-CoV-2 Delta (B.1.617.2) variant." *MedRxiv* preprint. https://doi.org/0.1101/2021.06.21.21259268; this version posted on June 25, 2021.
DOI: https://doi.org/10.1101/2021.06.21.21259268

[5] Y. Lee, P. Min, S. Lee, and S.W. Kim, "Prevalence and duration of acute loss of smell or taste in COVID-19 patients," *Journal of Korean Medical Science*, Vol. 35, e174, 2020.
DOI: https://doi.org/10.3346/jkms.2020.35.e174

[6] J.L. Frater, G. Zini, G. d'Onofrio, and H.J. Rogers, "COVID-19 and the clinical hematology laboratory," *International Journal of Laboratory Hematology*, Vol. 42, Suppl. 1, pp. 11-18, 2020.
DOI: https://doi.org/10.1111/ijlh.13229

[7] G. Lippi and M. Plebani, "The critical role of laboratory medicine during coronavirus disease 2019 (COVID-19) and other viral outbreaks," *Clinical Chemistry and Laboratory Medicine*, Vol. 58, No. 7, pp. 1063-1069, 2020.
DOI: https://doi.org/10.1515/cclm-2020-0240

[8] G. Lippi and M. Plebani, "Laboratory abnormalities in patients with COVID-2019 infection," *Clinical Chemistry and Laboratory Medicine*, Vol. 58, No. 7, pp. 1131-1134, 2020.
DOI: https://doi.org/10.1515/cclm-2020-0198

[9] R. Fang, X. Zheng, and M. Zhang, "Ethyl pyruvate alleviates early brain injury following subarachnoid hemorrhage in rats," *Acta Neurochirurgica*, Vol. 158, No. 6, pp. 1069-1076, 2016.
DOI: https://doi.org/10.1007/s00701-016-2795-3

[10] R. Garcia, J.M. Hernandez, M.D. Caballero, M. Gonzalez, J. Galende, M.C. del Canizo, L. Vazquez, and J.F. San Miguel, "Serum lactate dehydrogenase level as a prognostic factor in Hodgkin's disease," *British Journal of Cancer*, Vol. 68, No. 6, pp. 1227-1231, 1993.
DOI: https://doi.org/10.1038/bjc.1993.509

[11] B. Fialek, M. Pruc, J. Smereka, R. Jas, M. Rahnama-Hezavah, A. Denegri, A. Szarpak, M.J. Jaguszewski, F.W. Peacock, and L. Szarpak, "Diagnostic value of lactate dehydrogenase in COVID-19: A systematic review and meta-analysis," *Cardiology Journal*. Vol. 29, No. 5, pp. 751-758.

DOI: 10.5603/CJ.a2022.0056

[12] P. Mo, Y. Xing, Y. Xiao, L. Deng, Q. Zhao, H. Wang, Y. Xiong, Z. Cheng, S. Gao, K. Liang, M. Luo, T. Chen, S. Song, Z. Ma, X. Chen, R. Zheng, Q. Cao, F. Wang, and Y. Zhang, "Clinical characteristics of refractory COVID-19 in Wuhan, China*," Clinical Infectious Diseases*, Vol. 16, ciaa270, 2020.
DOI: 10.1093/cid/ciaa270

[13] D. Ferrari, A. Motta, M. Strollo, M. Locatelli, and G. Banfi, "Routine blood tests as a potential diagnostic tool for COVID-19," *Clinical Chemistry and Laboratory Medicine*, Vol. 58, pp. 1095-1099, 2020.
DOI: 10.1515/cclm-2020-0398

[14] Z. Zheng, F. Peng, B. Xu, J. Zhao, H. Liu, J. Peng, Q. Li, C. Jiang, Y. Zhou, S. Liu, C. Ye, P. Zhang, Y. Xing, H. Guo, and W. Tang, "Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis," *Journal of Infection*, Vol. 81, No. 2, pp. e16-e25, 2020.
DOI: 10.1016/j.jinf.2020.04.021

[15] J. Hu, J. Zhou, F. Dong, J. Tan, S. Wang, Z. Li, X. Zhang, H. Zhang, J. Ming, and T. Huang, "Combination of serum lactate dehydrogenase and sex is predictive of severe disease in patients with COVID-19," *Medicine (Baltimore)*, Vol. 99, No. 42, pp. e22774, 2020.
DOI: 10.1097/MD.0000000000022774

[16] H. Ward, C.J. Atchison, M. Whitaker, K.E.C. Ainslie, J. Elliott, L.C. Okell, R. Redd, D. Ashby, C.A. Donnelly, W. Barclay, A. Darzi, G. Cooke, S. Riley, P. Elliott, "Antibody prevalence for SARS-CoV-2 in England following first peak of the pandemic: REACT2 study in 100,000 adults," 2020. *MedRxiv* preprint.
DOI: https://doi.org/10.1101/2020.08.12.20173690.