RESEARCH ARTICLE

Features of α-HBDH in COVID-19 patients: A cohort study

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Abstract

Background: Coronavirus disease-2019 (COVID-19) has spread all over the world and brought extremely huge losses. At present, there is a lack of study to systematically analyze the features of hydroxybutyrate dehydrogenase (α-HBDH) in COVID-19 patients.

Methods: Electronic medical records including demographics, clinical manifestation, α-HBDH results and outcomes of all included patients were extracted.

Results: α-HBDH in COVID-19 group was higher than that in excluded group ($p < 0.001$), and there was no significant difference in α-HBDH before and after the exclusion of 5 patients with comorbidity in heart or kidney ($p = 0.671$). In COVID-19 group, the α-HBDH value in ≥61 years old group, severe group, and critical group, death group all increased at first and then decreased, while no obvious changes were observed in other groups. And there were significant differences of the α-HBDH value among different age groups ($p < 0.001$), clinical type groups ($p < 0.001$), and outcome groups ($p < 0.001$). The optimal scale regression model showed that α-HBDH value ($p < 0.001$) and age ($p < 0.001$) were related to clinical type.

Conclusions: α-HBDH was increased in COVID-19 patients, obviously in ≥61 years old, death and critical group, indicating that patients in these three groups suffer from more serious heart and kidney and other tissues and organs damage, higher α-HBDH value, and risk of death. The difference between death and survival group in early stage might provide a approach to judge the prognosis. The accuracy of the model to distinguish severe/critical type and other types was 85.84%, suggesting that α-HBDH could judge the clinical type accurately.

KEYWORDS
clinical features, coronavirus disease-2019, laboratory findings, respiratory infection

1 | INTRODUCTION

Since the outbreak of COVID-19 in December 2019, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), it has spread rapidly around the world. SARS-CoV-2 has attracted the attention of the global because of its high transmission ability, morbidity, and mortality.[1–4] On January 30, the World Health Organization

(WHO) identified COVID-19 as a public health emergency of international concern.[5] As of July 1, 2020, the number of confirmed cases of COVID-19 worldwide has reached 10,357,622, and the number of deaths has reached 508,055.[6]

Lactate dehydrogenase (LDH) is one of the important enzymes in glycolysis and gluconeogenesis. It mainly catalyzes the transformation between lactic acid and pyruvate. Its enzymatic reaction

is pyruvate $+NADH+H^+ \rightleftharpoons$ lactic acid $+NAD^+$. LDH consists of five isozymes composed of different combinations of H and M subunits: LDH1 (H4), LDH2 (H3M), LDH3 (H2M2), LDH4 (HM3), and LDH5 (M4). α-HBDH is tested by the α-ketoacid, a substrate, to determine the LDH activity. Additionally, the activity of LDH1 and LDH2 with more H subunits is described by α-HBDH activity because of the high affinity for this substrate to the H subunit in LDH. α-HBDH level increased in the progression of cor pulmonale, leukemia, and tumor. Moreover, the extents of the increase and the tissue and organ injury were closely related, which can be used as an auxiliary diagnostic index.[7-10] Studies had shown that higher LDH was one of independent high-risk factors for COVID-19 patients and was related to the severity of the disease.[11] α-HBDH and LDH are isozymes; their activity changes are consistent in most time. α-HBDH reflects the activity of LDH1 and LDH2, which is mainly distributed in the heart and kidney, the activity of the α-HBDH in the heart is more than half of the total enzyme activity,[12] so it is used to assess heart damage in clinical practice. COVID-19 could cause damage to the heart,[13] α-HBDH may reflect the changes of disease more sensitively than LDH in COVID-19 patients, and there is a lack of systematic and comprehensive research on the correlation between α-HBDH and COVID-19.

Compared with other pneumonia types, the α-HBDH level in COVID-19 patients was significantly higher, and the α-HBDH value of severe group was higher than that of non-severe group.[14,15] When complicated with cardiovascular disease or gastrointestinal symptoms, the increase of α-HBDH in COVID-19 patients was much more significant as well.[16,17] Cen et al. observed 1007 mild and moderate COVID-19 patients for 28 days. It was found that the higher the α-HBDH value, the greater the risk of progression to severe or critical type.[18] Zhang Gemin et al. divided 95 COVID-19 patients into four groups according to their α-HBDH level on admission. They found that the higher the α-HBDH value, the greater the proportion of severe cases, and the higher the risk of death or need for mechanical ventilation for patients, showing that the high α-HBDH level indicated an increased risk of further aggravation of the disease.[19] In this study, we compared the difference of α-HBDH between COVID-19 group and excluded group, compared the difference of α-HBDH before and after excluding patients with comorbidity in heart or kidney, and analyzed the changes of α-HBDH values of COVID-19 patients with different ages, clinical types, and outcomes. The effects of α-HBDH, age, and gender on the clinical type of COVID-19 patients were quantified by the optimal scale regression model, so as to achieve the purpose of early judging the severity of the disease.

2 | METHODS

2.1 | Study design

This research project was a bidirectional observational cohort study. This cohort established on February 9, 2020, all patients hospitalized in Xiangyang No.1 People's Hospital were included in this cohort before February 29, 2020. All information was traced back to the January 23, 2020. The last day of follow-up was on March 28, 2020.

According to the diagnosis and treatment guidelines,[20] we treated patients and divided patients into 3 groups: (1) COVID-19 group: patients with positive nucleic acid test; (2) clinical diagnosis group: patients with negative nucleic acid test or without nucleic acid test, but with imaging characteristic of viral pneumonia in pulmonary CT images; (3) excluded group: patients with negative nucleic acid test or without nucleic acid test, and without imaging characteristic of viral pneumonia in pulmonary CT images. The study was approved by the ethics review board of Xiangyang No.1 People's Hospital (No.2020GCP012) and registered at the Chinese Clinical Trial Registry as ChiCTR2000031088. Informed consent from patients has been exempted since this study is an observational cohort study that does not involve patients' personal privacy.

2.2 | Data collection

Two groups (two researchers per group) extracted the data from hospital information system through a consistent data collection protocol and cross-checked. Gender, age, comorbidity, all α-HBDH test results, disease onset date, outcome, death date, etc. were collected. A third expert was involved when there was disagreement. The data within the course of 1–30 days were statistic analyzed. We compared the difference of α-HBDH between COVID-19 group and excluded group, compared the difference of α-HBDH before and after excluding patients with comorbidity in heart or kidney to determine whether comorbidity will further affect α-HBDH in COVID-19 patients. For the COVID-19 patients, according to their age, they were divided into ≤40 years old group, 41–60 years old group and ≥61 years old group; according to the outcome, they were divided into death group and survival group; and according to the severity, they were divided into mild group, moderate group, severe group, and critical group. The distributions of α-HBDH median value were plotted with an 5-days interval (T1, T2, T3...Tn represented the time unit successively). The symptom onset data were designed as the first day of disease, the abnormal percentage, median, and quartile interval of α-HBDH in different ages, outcomes, and clinical types were calculated.

2.3 | α-HBDH examination

The α-HBDH test was conducted by Laboratory Department of Xiangyang No.1 People's Hospital. The reagent was α-Hydroxybutyrate Dehydrogenase Kit (α-ketobutyrate Substrate Method), the test instrument was automatic biochemical immunoassay analyzer (Abbott Laboratories ARCHITECT c16000), and the normal range of α-HBDH value was 72–182 U/L.

2.4 | Statistical analysis

All statistical analyses were performed by SPSS 20.0. Continuous data in accordance with normality were represented by means and

standard deviations, otherwise median (interquartile, IQR) was applied. Categorical data were described as frequency (%). The chi-square test was conducted to assess significance between groups. t test was used to compare the quantitative data of normal distribution between the two groups, and the comparison of the quantitative data of non-normal distribution between the two groups was analyzed using Mann-Whitney U test. The correlation between two variables was tested by Spearman correlation test. The maximum α-HBDH value in the first 15 days, age, and gender was regarded as independent variables, and clinical types were regarded as dependent variables to build the optimal scale regression model.

3 | RESULTS

This study included all of the 542 patients till February 29, 2020, of which the pharyngeal swab nucleic acid tests in 142 cases were positive, (9 cases that have data stored in other hospitals cannot be traced), and there were 262 patients included in excluded group.

3.1 | General information

A total of 142 cases were positive for nucleic acid test, among which the data of 9 cases were incomplete, 2 cases were infants; thus, 131 cases were included in COVID-19 group, including 63 males and 68 females, aged 50.13 ± 17.13 years old. Among them, there were 4 mild cases, 88 moderate cases, 18 severe cases, and 21 critical cases, and there 5 patients who were complicated with heart or kidney disease. The average time from onset to admission, from onset to discharge, from onset to death, and length of hospitalization were 4.54 ± 3.10, 26.87 ± 9.19, 18.4 ± 9.77, and 22.38 ± 8.70 days, respectively. In the first 30 days, the α-HBDH median value was 156.33 (124.00–222.08) U/L. In this study, 565 tests of α-HBDH were extracted from 37 laboratory indicators (including 24 560 outpatient and inpatient examination results), accounting for 2.30% of the total test results.

There were 262 cases in excluded group, in the first 30 days, the α-HBDH median value was 133.32 (115.58–162.96) U/L, without obvious changes during T1-T6, and there was significant difference in α-HBDH between excluded group and COVID-19 group ($p < 0.001$). After excluding 5 patients who were complicated with heart or kidney disease, the α-HBDH median value in these 126 patients was 154.75 (123.19–216.63) U/L, there was no significant difference in α-HBDH between the 126 patients and the original 131 patients in the first 30 days ($p = 0.671$).

3.2 | α-HBDH in different age groups of COVID-19 patients

In ≤40 years old group, 41–60 years old group and ≥61 years old group, the α-HBDH median value was 123.17 (106.94–144.95) U/L,

150.49 (120.18–185.20) U/L, and 221.59 (156.76–302.89) U/L, respectively, and the α-HBDH value abnormal percentage was 10.53%, 26.74%, and 60.70%, respectively. The changes indicated that the α-HBDH median value in ≤40 years old group increased during T1-T2 and decreased after T2, and the normal range was T1 to T6; in 41–60 years old group, the α-HBDH median value decreased during T1-T6 and was in the normal range from T1 to T6; in ≥61 years old group, the α-HBDH median value increased during T1-T2 and decreased after T2, and the abnormal time interval was T2-T5 (Figure 1, Table 1).

There were significant differences of the α-HBDH value in the first 30 days among the three age groups. Significant differences were observed in the α-HBDH value between ≤40 years old group and 41–60 years old group during T1-T4, between ≤40 years old group and ≥61 years old group during T1-T6, and between 41–60 years old group and ≥61 years old group during T2-T6. Differences were also significant in the α-HBDH value abnormal percentage among the three age groups ($p < 0.001$). The age was correlated with α-HBDH value according to the Spearman correlation test ($p < 0.001$), and the coefficient was 0.52.

3.3 | α-HBDH in different outcome groups of COVID-19 patients

In survival group and death group, the α-HBDH median value was 147.80 (121.55–194.67) U/L and 337.18 (294.01–477.11) U/L, respectively, and the α-HBDH value abnormal percentage was 29.52% and 96.08%, respectively. The changes indicated that the α-HBDH median value in survival group increased during T1-T2, decreased after T2, and was in the normal range during T1-T6, while in death group, the α-HBDH median value increased during T1-T4 and decreased after T4, and the abnormal time interval was T1-T6 (Figure 1, Table 2).

There were significant differences of the α-HBDH in the first 30 days and every time unit during T1-T6. Differences were also significant in the α-HBDH value abnormal percentage among the two outcome groups ($p < 0.001$). Spearman's correlation test showed that there was a correlation between outcome groups and the α-HBDH value ($p < 0.001$), and the correlation was 0.49.

3.4 | α-HBDH in different clinical type groups of COVID-19 patients

In mild group, moderate group, severe group, and critical group, the α-HBDH median value were 110.41 (105.67–120.25) U/L, 134.92 (114.40–163.23) U/L, 180.95 (144.02–231.01) U/L, and 293.57 (209.53–368.64) U/L, respectively, and the abnormal percentage of α-HBDH value was 0.00%, 12.45%, 49.47%, and 85.59%, respectively. The changes indicated that the α-HBDH median value of the moderate group increased during T1-T2 and decreased after T2 and was in the normal range during T1-T6; in the severe group,
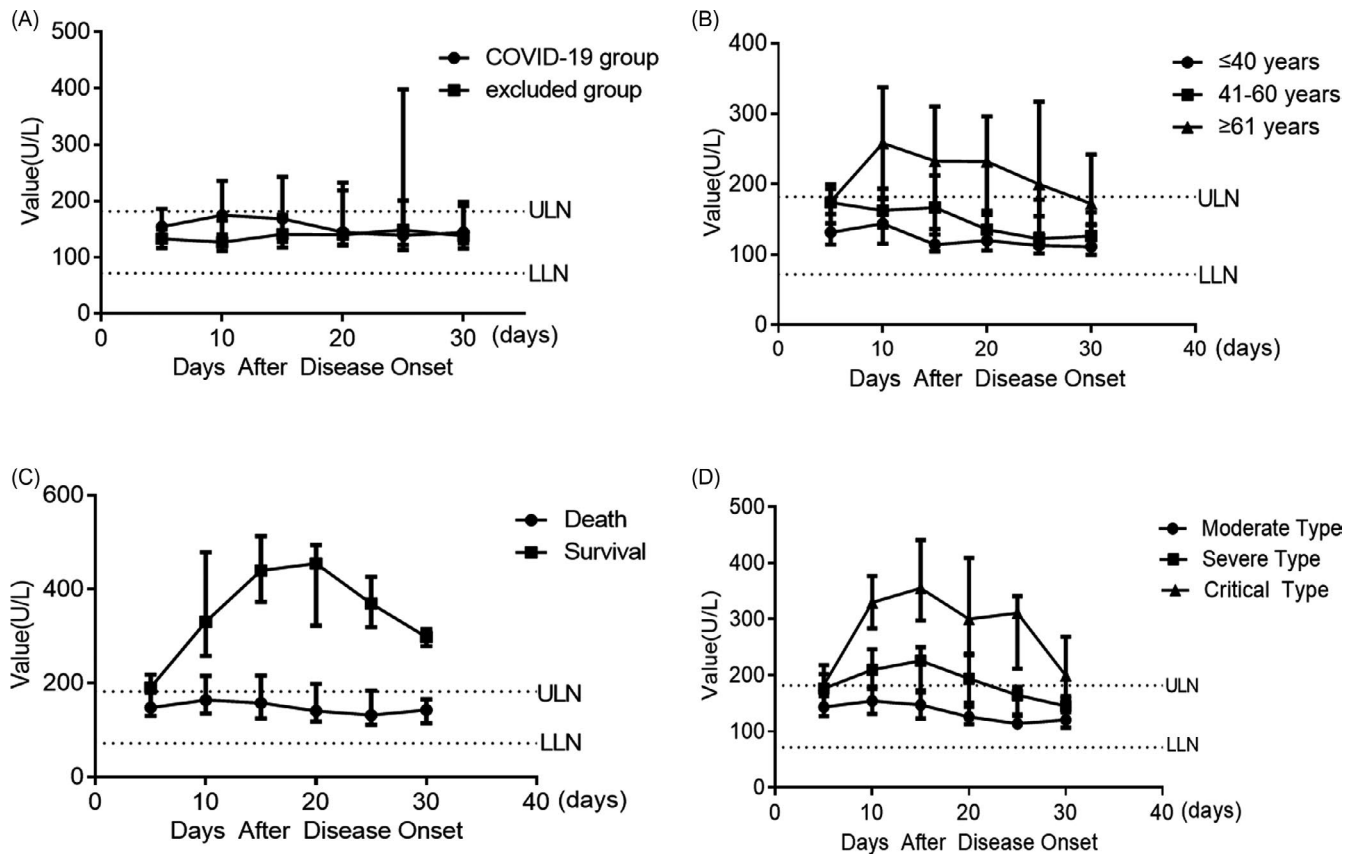
FIGURE 1 (A) α-HBDH in COVID-19 group and excluded group during total course, (B) α-HBDH in different age groups of COVID-19 patients, (C) α-HBDH in different outcome groups of COVID-19 patients, (D) α-HBDH in different clinical type groups of COVID-19 patients

the α-HBDH median value increased during T1-T3 and decreased after T3, and the abnormal time interval was T2-T4; in the critical group, the α-HBDH median value increased during T1-T3 and decreased after T3, and the abnormal time interval was T1-T6 (Figure 1, Table 3). However, the mild group was excluded in statistical analysis for the reason that it only contained 4 cases.

There were significant differences of the α-HBDH value in the first 30 days among the three clinical type groups. Significant differences were observed in the α-HBDH value between moderate type group and severe type group during T1-T6, between moderate type group and critical type group during T1-T6, and between severe type group and critical type group during T2-T6.

3.5 | Optimal scale regression model based on this study

After excluded 4 mild cases, we built the optimal scale regression model based on the maximum α-HBDH value in the first 15 days, age, gender, and clinical type. The adjusted R^2 of the model was 0.659. The clinical type was significantly correlated with age ($p < 0.001$) and α-HBDH value ($p < 0.001$), but not with gender ($p = 0.337$). The results were shown in Table 4. The model expression was Q_levels = 0.648*Q_α-HBDH + 0.036*Q_gender + 0.271*Q_age (Q_levels, Q_ages, Q_α-HBDH and Q_gender represent the scale

quantification scores of clinical type, age, α-HBDH value, and gender, respectively). The comparison between the output type and the actual type quantification score was shown in the Figure 2. According to the model, the output accuracy of moderate, severe, and critical types was 81.45% in this study. In order to discriminate moderate type and severe/critical type, the severe type and critical type were combined to the same category, and the accuracy was 85.84% in this study.

4 | DISCUSSION

α-HBDH is one of the important enzymes in the process of glucose metabolism, which is widely distributed in various tissues and organs, especially in the heart, brain, kidney, and red blood cells. COVID-19 causes damage to the heart and other tissues and organs, which results in the release of α-HBDH and the increase of α-HBDH in blood terminally.

α-HBDH median value in COVID-19 patients was higher than that in excluded group, and there was significant difference between them. The difference of α-HBDH median value between the two group was mainly in the first 20 days, in which the peak value of COVID-19 group appeared in T2, while the excluded group appeared no obvious changes (Figure 1). And the difference suggested that COVID-19 could cause heart and kidney damage, and led to the

TABLE 1 α-HBDH in different ages of COVID-19 patients

Period	≤40 years old (Group 1)			41–60 years old (Group 2)			≥61 years old (Group 3)			p value
	Median (IQR)	N	Abnormal Percentage (%)	Median (IQR)	N	Abnormal Percentage (%)	Median (IQR)	N	Abnormal Percentage (%)	
First 30 Days	123.17 (106.94–144.95)	133	10.53%	150.49 (120.18–185.20)	172	33.33%	221.59 (156.76–302.89)	201	60.70%	p1 < 0.001, p2 < 0.001, p3 < 0.001
T1	131.88 (114.41–144.56)	22	9.09%	174.2 (133.20–193.85)	21	35.00%	175.65 (157.75–199.68)	24	37.50%	p1 = 0.009, p2 < 0.001, p3 = 0.306
T2	144.25 (115.94–178.92)	34	23.53%	162.83 (138.83–193.96)	40	32.26%	258.66 (180.66–337.72)	40	70.00%	p1 = 0.044, p2 < 0.001, p3 < 0.001
T3	114.44 (104.92–136.48)	21	4.76%	167.29 (128.72–211.43)	31	17.24%	233.23 (162.08–310.66)	38	65.79%	p1 < 0.001, p2 < 0.001, p3 = 0.002
T4	120.07 (106.18–131.25)	28	3.57%	135.97 (118.59–156.72)	29	25.93%	232.36 (162.30–296.36)	39	69.23%	p1 = 0.015, p2 < 0.001, p3 < 0.001
T5	113.17 (101.75–129.70)	17	0.00%	122.83 (111.43–178.23)	27	12.50%	200.05 (154.75–317.27)	33	60.61%	p1 = 0.076, p2 < 0.001, p3 < 0.001
T6	111.57 (99.73–141.77)	11	18.18%	126.80 (111.96–160.15)	24	26.74%	172.36 (143.66–242.52)	27	48.15%	p1 = 0.303, p2 = 0.003, p3 < 0.001

P1: Group 1 vs. Group 2, P2: Group 1 vs. Group 3, P3: Group 2 vs. Group 3, N: Total times of test in this period.

TABLE 2 α-HBDH in different outcomes of COVID-19 patients

| Period | Survival | | | Death | | | |
	Median (IQR)	N	Abnormal percentage (%)	Median (IQR)	N	Abnormal percentage (%)	p value
First 30 Days	147.80 (121.55–194.67)	454	29.52	337.18 (294.01–477.11)	51	96.08	p < 0.001
T1	148.48 (130.85–180.97)	61	24.59	191.11 (181.58–218.19)	6	66.67	p = 0.014
T2	165.02 (135.92–215.63)	100	37.00	331.44 (258.94–479.36)	13	100.00	p < 0.001
T3	157.30 (125.68–214.05)	81	33.33	440.35 (373.28–513.89)	9	100.00	p < 0.001
T4	141.14 (118.86–198.90)	87	27.59	455.11 (322.65–426.79)	9	100.00	p < 0.001
T5	132.02 (112.06–184.22)	69	27.54	369.98 (319.60–426.79)	8	100.00	p < 0.001
T6	142.90 (113.74–165.30)	56	21.43	298.80 (279.30–315.31)	6	100.00	p < 0.001

N: Total times of test in this period.

increase of α-HBDH. In this study, there was no significant difference in the value of α-HBDH before and after the exclusion of 5 patients with comorbidity in heart or kidney, which meant the α-HBDH of these 5 patients had no significant effect on the overall data of COVID-19 group, and suggested COVID-19 induced the increase of α-HBDH. But due to the limited data, we could not perform a subgroup analysis between COVID-19 patients and COVID-19 patients with comorbidity in heart of kidney, whether the combination of heart or kidney diseases would further affect the α-HBDH in COVID-19 patients remains to be investigated.

In terms of the COVID-19 patients, the distribution and abnormal percentage of α-HBDH were significantly different in different age groups, outcome groups and clinical type groups (Figure 1). Age and outcome were significantly correlated with α-HBDH. Moreover, α-HBDH value may be related to the severity of COVID-19.

In ≥61 years old group and death group, the α-HBDH median value increased from T1 and reached a single peak in T2 (258.66 U/L) and T4 (455.11 U/L), respectively, which was significantly different from that in ≤40 years old group (peak value was 144.26 U/L), 41–60 years old group (peak value was 174.26 U/L) and survival group (peak value was 165.02 U/L). The abnormal interval of α-HBDH median value in ≥61 years old group and death group was T1-T5, T1-T6 respectively, which was significantly different from that in ≤40 years old group, 41–60 years old group and survival group, in which α-HBDH median value were all in the normal range. It shows that the older the age, the worse the outcome, the higher the α-HBDH value, and the longer the abnormal interval. The α-HBDH value in ≥61 years old group and death group was higher than that in other groups, indicating that the injury of heart, brain, kidney, and other tissues and organs is more serious in elderly and death patients, which was consistent with previous study.[21] This may be related to the poor function of the immune system and being more sensitive to virus damage in elderly and seriously ill patients. This characteristic suggests that we should pay more attention to elderly patients and patients of which α-HBDH continues to increase significantly. According to the data distribution and statistical analysis, the α-HBDH value can distinguish the death and the survival. For example, during T1, patients with α-HBDH ≥180.97 U/L have a ≥25% chance of survival, and patients with α-HBDH ≥218.19 U/L

have a ≥75% chance of death, which might have guiding significance for judgment of disease development in early stage. Enough cases and data could help us build a mathematic model and recognize the prognosis in advance better.

The α-HBDH median value of the mild group was in the normal range, without obvious change, indicating that the injury of tissue and organ injury in this type was slight. The same as mild group, α-HBDH median value in moderate group also distributed in the normal range. It increased firstly and reached a peak (133.20 U/L) in T2, indicating that tissue and organ injury occurred immediately after the symptom onset in spite of the slight degree and mainly occurred in the first 10 days. The changes of α-HBDH median value of severe group was similar to that of critical group, which increased during T1-T3 and decreased after T3. Their peak value was 222.56 and 355.23 U/L appearing in T3 and recovered to normal range in T5 and T7, respectively. It shows that the more serious the illness, the higher the α-HBDH median value and peak value, the longer the abnormal interval, which may be related to the serious virus-induced acute lung injury, tissues, and organs damage in severe and critical type groups. These characteristics are of great significance for us to judge the severity of the disease by α-HBDH.

The maximum α-HBDH value in the first 15 days, age, and gender of all patients were used to build the optimal scale regression model. α-HBDH <250.17 U/L and aged <60 years old was associated with moderate type, α-HBDH between 259.88–311.73 U/L and aged between 62–70 years old was associated with severe type, α-HBDH >327.71 U/L and aged >70 years old was associated with critical type. In this model, the output accuracy for clinical type was over 80%, which indicated that the model could distinguish the clinical classification based on our data well. α-HBDH and age could be used to discriminate the clinical type of COVID-19 patients. And if further verified by other data, it could help us to grasp the opportunity of treatment and reduce the risk of progression to severe and critical type in early stage.

However, this study has several limitations. All the patients in the study come from the single hospital, and the sample size is small. This study is a retrospective cohort study, which fails to detect and analyze the daily α-HBDH in patients and may lose some information.

TABLE 3 α-HBDH in different clinical types of COVID-19 patients

Period	Moderate type (group 1)			Severe type (group 2)			Critical type (group 3)			p value
	Median (IQR)	N	Abnormal percentage (%)	Median (IQR)	N	Abnormal percentage (%)	Median (IQR)	N	Abnormal percentage (%)	
First 30 Days	134.92 (114.40–163.23)	273	12.45	180.95 (144.02–231.01)	95	49.47	293.57 (209.53–368.64)	118	85.59	p1 < 0.001, p2 < 0.001, p3 < 0.001
T1	143.40 (127.33–178.20)	41	19.51	176.28 (143.43–201.95)	12	41.67	182.88 (163.28–218.19)	10	50.00	p1 = 0.046, p2 = 0.017, p3 = 0.468
T2	154.24 (130.94–179.86)	64	20.31	211.30 (176.44–245.47)	21	66.67	329.90 (281.99–396.87)	23	100.00	p1 < 0.001, p2 < 0.001, p3 < 0.001
T3	147.36 (123.09–169.97)	49	14.29	222.56 (159.52–248.88)	17	64.71	355.23 (297.57–440.91)	18	100.00	p1 < 0.001, p2 < 0.001, p3 < 0.001
T4	125.84 (113.13–143.89)	54	3.70	194.13 (151.50–235.97)	20	55.00	300.20 (238.58–408.87)	20	100.00	p1 < 0.001, p2 < 0.001, p3 < 0.001
T5	113.86 (108.60–129.70)	37	10.81	160.69 (120.62–174.69)	16	25.00	311.01 (211.61–340.84)	23	82.61	p1 = 0.008, p2 < 0.001, p3 < 0.001
T6	120.49 (106.79–143.89)	28	0.00	143.82 (126.68–156.23)	9	22.22	199.33 (158.84–268.88)	24	66.67	p1 = 0.306, p2 < 0.001, p3 = 0.007

P1: Group 1 vs. Group 2, P2: Group 1 vs. Group 3, P3: Group 2 vs. Group 3, N: Total times of test in this period.

TABLE 4 Variable Category and quantification score in optimal scale regression model

Variable	Classification	Frequency	Score
Clinical type	Moderate type	85	−0.545
	Severe type	21	0.207
	Critical type	18	2.332
α-HBDH (U/L)	96.20–109.35	5	−0.569
	113.28–182.50	64	−0.538
	187.30–250.17	28	−0.241
	259.88–311.73	8	0.118
	327.71–401.03	10	1.603
	441.09–833.00	9	2.921
Age	15.00–29.00	16	−0.627
	30.00–39.00	19	−0.627
	40.00–47.00	18	−0.627
	48.00–54.00	20	−0.627
	55.00–60.00	15	−0.566
	62.00–70.00	18	1.019
	71.00–90.00	18	1.997
Gender	Male	60	1.033
	Female	64	−0.968

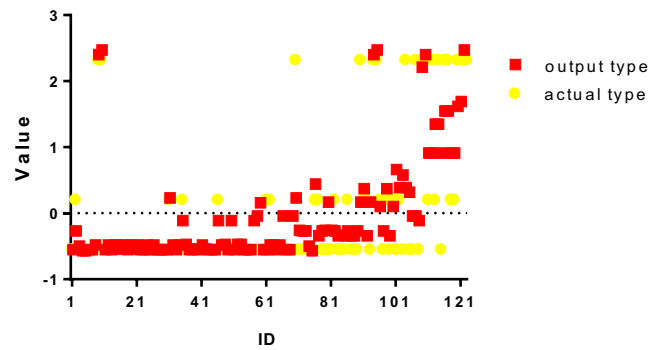Score: quantitative score in optimal scale regression model.

FIGURE 2 Comparison between the output type and the actual type quantification score in the model

5 | CONCLUSION

α-HBDH was increased in COVID-19 patients, obviously in ≥61 years old, death and critical group, indicating that patients in these three groups suffer from more serious tissues and organs damage, higher α-HBDH value and risk of death. The obvious difference between death and survival group in early stage may provide a approach to judge the prognosis. The accuracy of the model to distinguish severe/critical type and other types is 85.84%, suggesting that α-HBDH might judge the clinical type of COVID-19 patients accurately. In brief, α-HBDH is an important indicator to judge the severity and prognosis of COVID-19.

CONFLICT OF INTERESTS

All the authors declared that there were no conflict in this work and approved to publish this paper.

DATA AVAILABILITY STATEMENT

The data that supported the findings of this study are available from the corresponding author upon reasonable request.

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