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Association between serum lactate dehydrogenase and 60-day mortality in Chinese Hakka patients with acute myeloid leukemia: A cohort study

Zuomiao Xiao[1] ⓘ | Rongpeng Gong[2] | Xianchun Chen[1] | Dejun Xiao[1] | Shi Luo[1] |
Yanhong Ji[3]

[1]Department of Clinical Laboratory, The Affiliated Ganzhou Hospital of Nanchang University, Ganzhou, China

[2]Medical College of Qinghai University, Xining, China

[3]Department of Immunology& Microbiology, School of Medicine, Xi'an Jiaotong University, Xi'an Shaanxi, China

Correspondence
Yanhong Ji, Department of Immunology& Microbiology, School of Medicine, Xi'an Jiaotong University, Xi'an Shaanxi, China.
Email: jiyanhong@xjtu.edu.cn

Abstract

Background: There is evidence that a high level of serum lactate dehydrogenase (LDH) is associated with poorer overall survival in acute myeloid leukemia (AML), but its link to 60-day mortality of AML remains unclear.

Methods: All patients newly diagnosed with AML were included in this cohort study. LDH was measured for the first time after admission. Multivariable logistic regression was used to explore the association between serum LDH and 60-day mortality. Interaction and stratified analyses were conducted including age, sex, albumin, glucose, myoglobin, and standard chemotherapy.

Results: Three hundred and seventy-one patients ≥15 years of age, who were newly diagnosed with AML, were consecutively selected. The total prevalence of 60-day mortality was 27.2% (101/371), while it was 32.1% (42/131) and higher than in the LDH ≥570U/L compared with the LDH<570U/L, with the prevalence of 24.6% (59/240); however, the difference was not statistically significant. In multivariate regression models, odd ratios and corresponding 95% confidence intervals (CIs) for Log_2 and twice limit of normal (ULN) of LDH were 1.46 (1.0, 2.14) and 2.76 (1.24, 6.16), respectively. Interaction analysis revealed no interactive role in the association between LDH concentration and 60-day mortality.

Conclusions: Serum LDH level was associated with 60-day mortality, especially for the patients with LDH ≥570U/L.

KEYWORDS
acute myeloid leukemia (AML), lactate dehydrogenase (LDH), 60-day mortality

1 | INTRODUCTION

Acute myeloid leukemia (AML) is the most common form of acute leukemia in adults, and it is 3–4 times more common in adults than in those with acute lymphocytic leukemia (ALL). AML is a disorder characterized by clonal proliferation derived from primitive hematopoietic stem cells or progenitor cells.[1,2] Abnormal differentiation of myeloid cells results in a high level of immature malignant cells and

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Correction added on 24th November 2021, after first online publication: Notes and abbreviations have been inserted in Table 3

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fewer differentiated red blood cells and platelets. Sixty-day mortality is defined as a patient dying from any cause within 60 days of hospitalization with AML,[3,4] However, 60-day mortality remains a significant problem and physicians have devoted much effort to avoiding it;[5] nevertheless, it has not yet been adequately addressed. Serum lactate dehydrogenase (LDH) levels are often used to diagnose disease and prognosis of hematological malignancies, such as AML, myelodysplastic syndromes (MDS), or multiple myeloma.[6,7] LDH level is inversely associated with medical prognosis in patients with AML. However, the association between LDH level and 60-day mortality, especially in hospitalized patients with AML, is limited. Moreover, we did not find a similar study in the Chinese Hakka population. Until now, there are as many as 100 million Hakka populations in the world; Ganzhou is one of the important settlement cities with nearly 10 million Hakka people. However, there is no relevant study among these special populations. Therefore, this study aimed to investigate the association between LDH and 60-day mortality in a sample of the Hakka population with AML.

2 | METHODS

2.1 | Study Design and Participants

The present retrospective cohort study included consecutive patients who were newly diagnosed with primary AML and treated and evaluated at the Affiliated Ganzhou Hospital of Nanchang University (Jiangxi Province, China) between January 1, 2013 and May 31, 2020. Ganzhou city, located in the south of Jiangxi Province, is the largest prefecture-level city with the largest population in Jiangxi Province and a gathering place for the Hakka people. All individuals in this study underwent bone marrow aspiration and had confirmed AML diagnosis based on the morphological picture and immunophenotype analysis, according to the World Health Organization (WHO) classification system (version 2016).[8] Patients diagnosed with acute promyelocytic leukemia (APL) were excluded because their management and treatment differ from other AML subtypes. Individuals with secondary AML were also excluded. These patients had a history of other hematological malignancies, such as chronic myelogenous leukemia (CML) and MDS, because the primary disease may affect the concentration of serum LDH. The mixed phenotype acute leukemia (MPAL) and those who suffered from AML-M6, should be diagnosed with MDS according to WHO classifications (Version 2016), were excluded due to non-AML patients in the strict sense.[8]

Additionally, patients who were younger than 15 years of age, had not undergone serum LDH test, or had an uncertain survival status (lost to follow-up) were also excluded. All of the remaining patients were included in the study with or without chemotherapy (Figure 1). No patient underwent bone marrow transplantation in 60 days after admission. Sixty-day mortality was defined as death from any cause within 60 days of hospitalization with AML.[3,4] The final cohort included 371 AML patients, who were classified into four subgroups: AML-M$_2$, AML-M$_4$, AML-M$_5$, and other subgroups. The other subgroup included 35 patients, classified as follows: AML-M$_0$ (n = 3), AML-M$_1$ (n = 23), AML-M$_6$ (n = 2), and AML-M$_7$ (n = 7). The study adhered to the principles of the Declaration of Helsinki and was approved by the Ethics Review Board of the Affiliated Ganzhou Hospital of Nanchang University. Given the retrospective nature of the study and use of anonymized patient data, requirements for informed consent were waived.

2.2 | Data collection and measurements

Data, including survival status, were collected from the electronic medical record system or follow-up telephone calls. Baseline examinations included blood and bone marrow parameters. Biomarkers included white blood cell (WBC) count, hemoglobin (Hgb), platelets (PLT), fibrinogen (Fg), DDimer (DD), direct bilirubin (DBIL), albumin (ALB), alanine aminotransferase (ALT), aspartate aminotransferase (AST),total bile acid (TBA),creatine kinase isoenzyme MB (CK-MB), myoglobin (MYO), creatinine (Crea), uric acid (UA), LDH, glucose (Glu), and bone marrow(BM) blast. All laboratory data were obtained from the initial examination of AML patients tested within 48 hours of admission, without anti-leukemia therapy. These parameters comprise routine testing, commonly used to evaluate the patient's physical condition, including liver, kidney, cardiovascular, and coagulation functions.

2.3 | LDH

Serum LDH was measured using a biochemical analyzer (AU5800, Beckman Coulter, Inc.) with LDH test reagent (Chongqing Zhongyuan Biological Co., Ltd); the reference interval for LDH was 80–285 U/L, in accordance with the national standard. Commercially available control materials for internal quality control (IQC) (Bio-Rad Laboratories, Inc. Hercules, CA, USA) were required for testing blood samples every day. The LDH parameter was included in the activities of external quality control (EQA), which was organized by the National Center for Clinical Laboratories (NCCL) twice per year, and criteria for feedback reports were fulfilled during this study. All data from this study, including LDH and other items/parameters, were the first test results of patients after admission due to AML.[9] LDH level was categorized into two groups according to the upper limit of normal (ULN): <570 U/L and ≥570 U/L.[10]

2.4 | Statistical analysis

Data are expressed as mean ±standard deviation (SD) or median (quartile 1–quartile 3 [i.e., interquartile range (IQR)]) for continuous variables, and as frequency or percentage for categorical variables. For baseline characteristics analysis, data were compared using the Mann–Whitney test for continuous variables and the chi-squared test for categorical variables. Logistic regression analysis

FIGURE 1 Flowchart of patient selection. Abbreviations: AML, acute myeloid leukemia; MPAL, mixed phenotype acute leukemia; MDS, myelodysplastic syndrome; t-AML, therapy-related AML
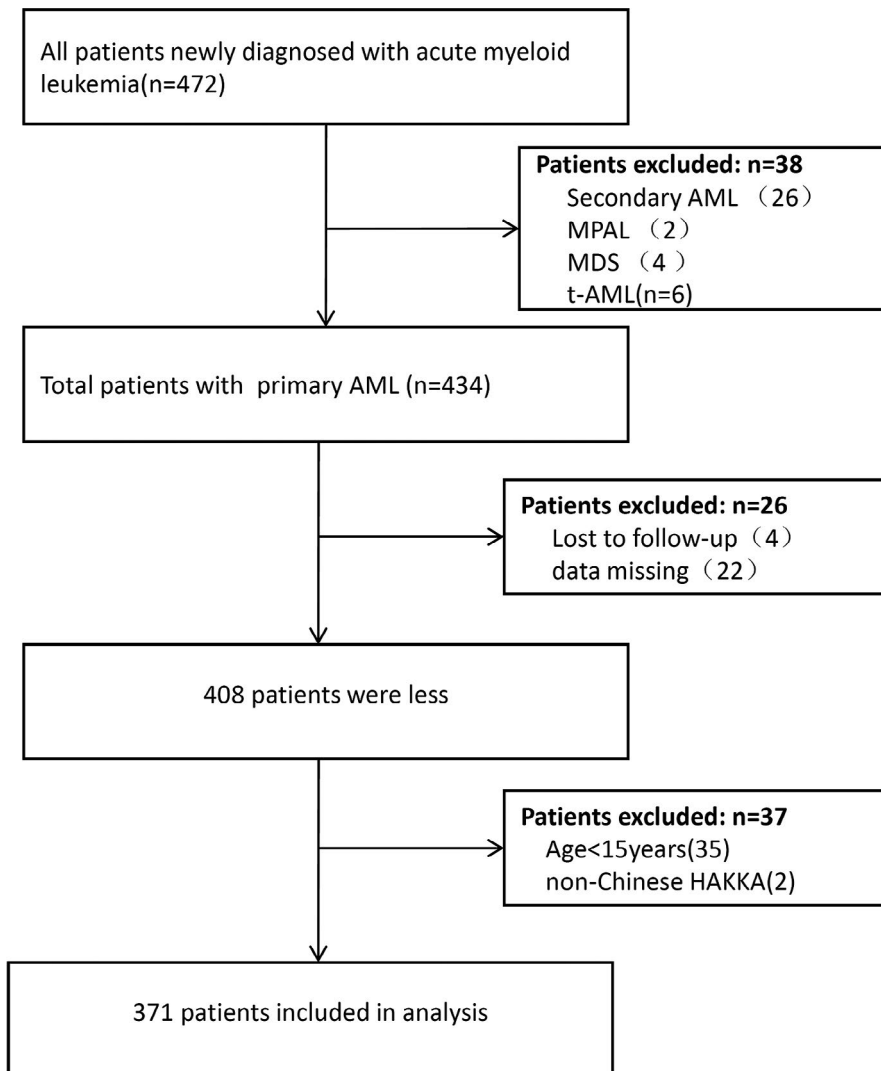
was used to estimate the odds ratio (OR) and corresponding 95% CI for the risk for ED rate (EDR) according to serum LDH levels.

Both nonadjusted and multivariate-adjusted models were used. Variables were selected as adjustment, if the matched odds ratio would change by at least 10%. Results were adjusted for age and sex in model I. To investigate independent associations, variables including age, sex, WBC count, Hgb, PLT, BM blasts, Fg, DD, and FAB classification were adjusted for subgroups in model II. Finally, age, sex, WBC, Hgb, PLT, BM blasts, Fg, DD, and FAB subtype, ALT, AST, ALB, DBIL, Crea, UA, CK-MB, MYO, TBA, and GSP were adjusted in model III.

Analyses stratified according to the result of univariate analysis (P-value lower than 0.005), including sex, age, ALB, Glu, MYO, and standard chemotherapy, examine the effect of these factors on the above associations. The likelihood ratio test was used to assess effect modification according to pre-specified subgroups used interaction terms between subgroup indicators and LDH. Interactions across subgroups were also tested using likelihood ratio tests. All analyses were performed using R 3.3.2 (http://www.R-project.org, The R Foundation) and Free Statistics

version 1.3. Differences with a two-sided $p < 0.05$ were considered to be statistically significant.

3 | RESULTS

Baseline characteristics of the study participants according to LDH categories are summarized in Table 1. Of 472 patients with AML, 371, who fulfilled the inclusion criteria, were identified (Figure 1). The median LDH level was 444.0 U/L (range 113–4978.9 U/L; IQR 272.–746.5 U/L). The median age of the patients was 59.0 years (range 15–94 years). Overall, 193 (52.0%) patients were male and 178 (48.0%) were female. In addition, there were 235 (63.3%) patients who accepted standard chemotherapy(a combination of cytarabine and anthracycline "7+3" or a combination of cytarabine and the other),[11] and 136 (36.7%) patients who did not accept the standard chemotherapy (including 51 patients who accepted single chemotherapy, only used decitabine or hydroxyurea, 85 patients did not accept any chemotherapy); 101 (27.2%) patients experienced 60-day death. Patients in the LDH ≥570 U/L group exhibited a higher level

TABLE 1 Baseline characteristics of the study participants

Variables	Total (n = 371)	LDH<570 U/L (n = 240)	LDH≥570 U/L (n = 131)	P-value
Sex, n (%)				0.042
Male	193 (52.0)	115 (47.9)	78 (59.5)	
Female	178 (48.0)	125 (52.1)	53 (40.5)	
Age(years)	59.0 (44.0, 68.0)	60.5 (47.0, 69.0)	54.0 (41.0, 65.0)	0.003
FAB subtype, n (%)				0.005
AML-M2	164 (44.2)	119 (49.6)	45 (34.4)	
AML-M4	51 (13.7)	29 (12.1)	22 (16.8)	
AML-M5	121 (32.6)	66 (27.5)	55 (42.0)	
Others	35 (9.4)	26 (10.8)	9 (6.9)	
Pulmonary infection, n (%)				0.347
No	158 (42.6)	107 (44.6)	51 (38.9)	
Yes	213 (57.4)	133 (55.4)	80 (61.1)	
Standard chemotherapy, n (%)				0.503
No	137 (36.9)	87 (36.2)	50 (38.2)	
Yes	234 (63.1)	153 (63.7)	81 (61.8)	
60-day mortality, n (%)				0.154
No	270 (72.8)	181 (75.4)	89 (67.9)	
Yes	101 (27.2)	59 (24.6)	42 (32.1)	
WBC, n (%)				< 0.001
$<10\times10^9$/L	145 (39.1)	124 (51.7)	21 (16.0)	
$\geq10\times10^9$/L	226 (60.9)	116 (48.3)	110 (84.0)	
Hgb(g/L)	66.0 (53.0, 82.5)	65.0 (51.0, 81.0)	69.0 (55.5, 83.0)	0.396
PLT($\times10^9$/L)	38.0 (18.0, 70.0)	40.0 (19.0, 74.2)	35.0 (16.0, 65.0)	0.407
BM Blast (%)	59.0 (39.1, 76.5)	58.7 (38.0, 74.8)	60.0 (39.9, 78.0)	0.229
Fg(g/L)	3.5 ± 1.4	3.7 ± 1.3	3.3 ± 1.4	0.026
DD (mg/L)	1.6 (0.8, 4.2)	1.4 (0.7, 3.3)	2.2 (1.0, 6.0)	< 0.001
DBIL (umol/L)	3.7 (2.6, 5.4)	3.7 (2.6, 5.3)	3.6 (2.6, 5.7)	0.424
ALB(g/L)	36.5 ± 5.0	36.2 ± 5.0	37.1 ± 4.9	0.106
ALT(U/L)	18.0 (12.0, 29.5)	15.6 (11.4, 27.1)	22.4 (14.0, 31.6)	< 0.001
AST(U/L)	24.0 (16.7, 35.0)	19.2 (15.0, 28.8)	32.0 (24.0, 45.0)	< 0.001
TBA (umol/L)	5.2 (3.0, 9.4)	5.0 (2.9, 8.2)	6.0 (3.4, 10.8)	0.058
Crea (umol/L)	69.2 (56.1, 89.0)	68.0 (54.3, 84.0)	74.8 (60.6, 97.8)	0.001
UA (mmol/L)	326.0 (242.0, 431.5)	296.0 (223.0, 387.5)	361.0 (283.5, 480.5)	< 0.001
GSP (mmol/L)	1.4 (1.3, 1.6)	1.4 (1.3, 1.6)	1.5 (1.3, 1.6)	0.445
GLU (mmol/L)	6.0 (5.3, 7.1)	6.0 (5.3, 7.0)	6.0 (5.2, 7.4)	0.579
LDH (U/L)	444.0 (272.3, 746.5)	306.5 (222.4, 420.2)	990.0 (726.5, 1380.0)	< 0.001
CK-MB (U/L)	10.2 (6.4, 15.7)	8.9 (5.7, 12.6)	13.6 (8.8, 25.2)	< 0.001
MYO (ng/ml)	20.0 (17.8, 34.1)	20.0 (16.6, 30.6)	23.3 (19.3, 44.5)	0.017

Note: data presented are mean±SD, median (Q1-Q3), or N (%).

Abbreviations: ALB, albumin; ALT, alanine aminotransferase; AML, acute myeloid leukemia; AST, aspartate aminotransferase; BM, bone marrow; CK-MB, creatine kinase isoenzyme MB; Crea, creatinine; DBIL, direct bilirubin; DD,D-dimer; FAB, French, American, British; Fg, fibrinogen; Glu, glucose; GLU, glucose; GSP, glycated serum protein; Hgb, hemoglobin; LDH, lactate dehydrogenase; MYO, myoglobin; PLT, platelet; TBA, total bile acid; UA, uric acid; WBC, white blood cell.

of DD, ALT, AST, UA, and CK-MB compared with those with LDH <570 U/L ($p < 0.001$). The 60-day mortality in the LDH ≥570 U/L group was higher than that in the <570 U/L group; However, the difference was not statistically significant ($p = 0.154$). Furthermore, patients in the LDH ≥570 U/L group were younger than those in the <570 U/L group ($p = 0.003$).

TABLE 2 Univariate analysis of risk factor associated with 60-day mortality in patients with AML

Variables	OR (95%CI)	P-Value
Sex		
Male	Ref.	
Female	0.63 (0.39~1)	0.049
Age	1.05 (1.03~1.07)	<0.001
FAB subtype		
AML-M2	Ref.	
AML-M4	0.61 (0.28~1.31)	0.204
AML-M5	0.78 (0.46~1.34)	0.377
Others	1.87 (0.88~3.95)	0.103
Pulmonary infection		
No	Ref.	
Yes	1.49 (0.93~2.39)	0.099
Chemotherapy		
Standard dose	Ref.	
Non-standard dose	0.08 (0.04~0.13)	<0.001
WBC		
$<10\times10^9$/L	Ref.	
$\geq10\times10^9$/L	0.87 (0.54~1.38)	0.546
HGB	0.99 (0.98~1.00)	0.236
PLT	1.0(0.99~1.01)	0.231
Blast	1.0 (0.99~1.01)	0.496
Fg	0.94 (0.79~1.11)	0.464
DD	1.01 (0.99~1.03)	0.323
DBIL	1.05 (1.01~1.10)	0.031
ALB	0.88 (0.84~0.93)	<0.001
ALT	1.00(1.0~1.0)	0.853
AST	1.00(1.0~1.01)	0.146
TBA	1.00 (0.99~1.02)	0.898
Crea	1.00 (1.0~1.01)	0.072
UA	1.0 (1.00~1.00)	0.975
GSP	1.38 (0.66~2.89)	0.389
Glu	1.22 (1.09~1.36)	<0.001
LDH (Log$_2$)	1.13 (0.91~1.41)	0.273
CK-MB	1.00 (0.99~1.01)	0.949
MYO	1.01 (1.0~1.01)	0.005

Abbreviations: ALB, albumin; ALT, alanine aminotransferase; AML, acute myeloid leukemia; AST, aspartate aminotransferase; CK-MB, creatine kinase isoenzyme MB; Crea, creatinine; DBIL, direct bilirubin; DD,D-dimer; FAB, French, American, British; Fg, fibrinogen; Glu, glucose; GSP, glycated serum protein; Hgb, hemoglobin; LDH, lactate dehydrogenase; MYO, myoglobin; PLT,platelet;BM, bone marrow; TBA,total bile acid; UA, uric acid; WBC, white blood cell.

Univariate analysis of risk factors associated with 60-day mortality in AML patients, reported as ORs and 95% CIs for the risk of that among patients with AML is summarized in Table 2. Glucose, albumin, age, levels, and the factor accepted standard chemotherapy were significantly associated with 60-day

mortality (p<0.001). Other factors, including Hgb, platelets, and other biomarkers, were not significantly associated with that (Table 2).

3.1 | Multivariate logistic regression analysis of LDH on the ED in AML

The ORs and corresponding 95% CIs for the risk for 60-day mortality according to serum LDH (Log$_2$) and LDH ≥570 U/L are summarized in Table 3. The risk for 60-day mortality increased for the group with LDH ≥570 U/L, with a nonadjusted OR of 1.45 (95%CI 0.91–2.32), compared with the group with LDH <570 U/L. After adjusting all covariates, the OR and 95% CI was 2.76 (1.24–6.16). The statistical results were robust among all models (Table 3).

3.2 | Subgroup analyses

To detect whether the association between serum LDH levels and 60-day mortality of AML was present in different subgroups, analyses and interactive analyses were stratified according to the result of univariate analysis (if p-value <0.005, selected) (Table 4). No variable played an interactive role in the association between LDH and incident EDR in AML (P for interaction >0.05). Nevertheless, in the LDH ≥570 U/L subgroup, with age ≥60 years, ALB<35g/L, Glu≥6.0mmol/L, MYO>20ng/L, or nonaccepted standard dose of chemotherapy were associated with a greater risk for 60-day mortality compared with the corresponding subgroup. Subgroup analyses were adjusted for sex, age, Hgb, WBC, PLT, bone marrow blast, Fg, DD, DBIL, TBA, AST, UA, ALT, CK-MB, MYO, ALB, creatinine levels, GSP, FAB subtype, and standard chemotherapy (Table 4).

4 | DISCUSSION

In this cohort study, serum LDH (Log$_2$) level was found to be associated with an elevated risk for 60-day mortality among patients with AML, independent of sex, age, WBC, PLT, Hgb, bone marrow blast, Fg, DD, DBIL, ALB, AST, ALT, TBA, GLU, Crea, UA, and CK-MB. Consistent results were found in the serum LDH ≥570 U/L group compared with the LDH <570 U/L group, and the results demonstrated that they were robust with no adjustment or a gradual adjustment. Furthermore, leukocyte count can be extremely elevated, normal, or extremely low in the peripheral blood of patients with AML; however, anemia and thrombocytopenia are frequently present.[12] In this study group, WBC count, which ranged from 0.29×10^9/L to 539.6×10^9/L, varied widely. Hence, WBC count, one of the adjusted factors, was used after being categorized into two groups: WBC ≥10×10^9/L and WBC <10×10^9/L.

The definition of early mortality in AML was different in different study; it is defined as death ≤60 days from diagnosis or after the start of chemotherapy.[3,4] The high early mortality remains a

TABLE 3 Multivariate logistical regression for LDH on 60-day mortality of AML.

Variable	Nonadjusted Model OR (95% CI)	Model I OR (95% CI)	Model II OR (95% CI)	Model III OR (95% CI)
LDH (log$_2$)	1.13(0.91~1.41)	1.30 (1.02~1.66)	1.48 (1.20~1.97)	1.46 (1.0~2.14)
Binary variable				
LDH<570 U/L	Ref.	Ref.	Ref.	Ref.
LDH≥570 U/L	1.45 (0.91~2.32)	1.94 (1.15~2.45)	2.85 (1.45~5.59)	2.76 (1.24~6.16)

Notes: ModelI:Adjusts for sex + age; Model II:adjusts for Model I+WBC+ Hgb+ PLT+BM Blast+ Fg+ DD+ FAB subtype; Model III: adjusts for Model II+ DBIL+ ALB+ALT+ AST+ TBA+ Crea+ UA+ GSP +Glu+ MYO+ Standard chemotherapy+ Pulmonary infection.

Abbreviations: LDH, lactate dehydrogenase; WBC, white blood cell; Hgb, hemoglobin; PLT , platelet; BM, bone marrow; Fg, fibrinogen; DD, D-dimer; FAB, French, American, British; DBIL, direct bilirubin; ALB, albumin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBA, total bile acid; GLU, glucose; MYO, myoglobin.

TABLE 4 Subgroup analyses of the association between serum LDH levels and 60-day mortality of AML.

Subgroups	n	60-day mortality LDH<570 U/L	LDH≥570 U/L	OR (95%CI)	P for interaction
Sex					0.944
Male	193	34 (29.6)	27 (34.6)	2.95 (1.08~8.06)	
Female	178	25 (20.0)	15 (28.3)	4.31 (1.09~17.05)	
Age(years)					0.570
<60	193	16 (13.9)	14 (17.9)	2.34 (0.75~7.26)	
≥60	178	43(34.4)	28 (52.8)	3.79 (1.16~12.34)	
ALB(g/L)					0.676
<35	130	31 (36.5)	20 (44.4)	5.39 (0.98~29.29)	
≥35	241	28 (18.1)	22 (25.6)	2.05 (0.77~5.42)	
Glu(mmol/L)					0.748
<6.0	180	19 (16.2)	15 (23.8)	4.37 (1.37~13.96)	
≥6.0	179	38 (33.3)	26 (40.0)	1.72 (0.58~5.1)	
MYO (ng/ml))					0.104
<20	109	11 (14.7)	6 (17.6)	0.66 (0.07~5.98)	
≥20	250	45 (28.5)	34 (37.0)	3.82 (1.56~9.39)	
Standard chemotherapy					0.694
No	137	46 (52.9)	33 (66.0)	2.82 (0.89~8.95)	
Yes	234	13 (8.5)	9 (11.1)	2.33 (0.73~7.41)	

Note: Adjusts for - sex+age+ FAB subtype+WBC+HGB+PLT+ALB+GSP+ Glu+CK-MB+MYO+BM Blast+standard chemotherapy+pulmonary infection.

Abbreviations: AML, acute myeloid leukemia; BM, bone marrow; CK-MB, creatine kinase isoenzyme MB; FAB, French, American, British; Glu, glucose; GSP, glycated serum protein; Hgb, hemoglobin; LDH, lactate dehydrogenase; MYO, myoglobin; PLT, platelet ALB, albumin; WBC, white blood cell.

clinical problem, and hematologists struggle to lower the risks of early mortality. To truly reflect the early mortality of AML patients in real world, we included all newly diagnosed AML patients and evaluated the mortality rate within 60 days after admission, so as to reduce sample loss and EDR calculation bias caused by admission criteria. In our study, the 60-day mortality was 27.2%, while 21–37.5% reported by previous study.[3,4,6,13] The results are similar. However, 60-day mortality of our study was slightly different from previous studies. In the previous study, patients who had accepted chemotherapy were included[6,14] and those AML patients who did not accept chemotherapy were excluded. Among these excluded patients, most of them were not in enough good condition to accept anti-leukemia treatment, due to comorbidities.[4] For example, some patients suffered from cerebral hemorrhage or acute myocardial infarction, they died so quickly that those patients had no opportunity to accept chemotherapy, these patients would be excluded subjectively, so the early mortality might have been reduced and lower that in the real world. Furthermore, the causes of early mortality of AML are complicated and unclear, even though, the hematologists have been managing to work something out.

Usually, they evaluate the risk with laboratory data and clinical performance status. Former studies show high concentration of LDH, and age is associated with a high risk for early mortality in AML patients.[10,15,16] Increased LDH levels are the product of the enhanced glycolytic activity of the tumor and tumor necrosis due to hypoxia, the latter being related to a high tumor burden.[10] Most previous studies have indicated that serum LDH is an independent prognostic factor for patients with AML (non-APL);[3,4,17] the higher the serum LDH level, the shorter the survival time.[6,7] There were some limitations with previous studies, those studies investigating the association between LDH and early mortality did not take into account patient functions of vital organs at admission.[7,18] In this case, our study considered several synergistic factors. These synergy factor laboratory data, including ALT, creatinine, and CK-MB, are used by physicians to comprehensively evaluate whether patients have normal liver, kidney, and cardiac function. Furthermore, all patients ≥15 years of age were also included in our study regardless of whether they received standard chemotherapy. In this way, the study may be more objective and comprehensive to learn whether serum LDH has an impact on early mortality in AML. Interestingly, the statistical results in our study were robust, both nonadjusted and adjusted models; these results are similar to previous studies that LDH is a prognostic factor for AML.[4,16] In particular, the effect was more obvious in those with LDH ≥570 U/L, and such a result may remind the clinicians of devoting more attention and more care to these AML patients.

There were some limitations to this retrospective study. First, some patients might not be included, because they died so quickly that doctors did not have enough time to perform bone marrow puncture, which precluded confirmation of the type of acute leukemia, even though they might be diagnosed with acute leukemia according to both blood film and clinical performance (approximately one or two patients per year). Second, this is a retrospective study; the data were collected from 2013 to 2021 (over an eight-year period), and the date of death data for some patients was obtained by telephone follow-up and may be biased. To reduce the bias, we conducted interviews with at least to two or three family members to determine the exact survival time of the patients. Furthermore, different batches of LDH reagents will affect test results to some degree. To make the value dependable, IQC is required every day to ensure that the result is under control before testing clinical specimens. We also take part in an external quality assessment that is organized by the NCCL each year to ensure the accuracy of the testing results. Fortunately, they satisfied both control results. Meanwhile, the instrument is required to undergo calibration twice per year as part of regular maintenance. Therefore, all testing results were dependable.

5 | CONCLUSION

Among a sample of the Chinese Hakka population, individuals ≥15 years of age with serum LDH ≥570 U/L were significantly associated with a higher risk for 60-day mortality in AML. In summary, we demonstrated that serum LDH was independently associated with an increased risk for 60-day mortality among Chinese patients with AML. Further research is needed to more definitively characterize the role of serum LDH for timely prevention of 60-day mortality in AML patients. This is significant and practicable because determining serum LDH level is usually a routine test requiring only a short time.

CONFLICT OF INTEREST

The remaining authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Zuomiao Xiao and Yanhong Ji designed this study and wrote the report. Rongpeng Gong took part in statistical analysis. Xianchun Chen, Shi Luo, and Dejin Xiao collected the clinical data. All authors reviewed and edited the report and have seen and approved the final draft.

DATA AVAILABILITY STATEMENT

The raw data required to reproduce these findings cannot be shared at this time as the data also form part of an ongoing study. If necessary, some or all data generated or used during the study are available from the corresponding author by request.

ORCID

Zuomiao Xiao https://orcid.org/0000-0002-6852-3372

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