Original Article

Elevated serum AST and LDH levels are associated with infant death in premature babies with neonatal leukemoid reaction: a cohort study

Ruibo Liu[1,2]^, Yuwen Huang[1], Zhifang Jia[3], Mary Joseline Joseph[1], Kening Chai[1,2], Tianhui Xiong[1,2], Wei Zhou[1,2], Linlin Qu[1], Wei Xia[2]

[1]Department of Laboratory Medicine, the First Hospital of Jilin University, Changchun, China; [2]College of Medical Technology, Beihua University, Jilin, China; [3]Division of clinical epidemiology, the First Hospital of Jilin University, Changchun, China

Contributions: (I) Conception and design: L Qu; (II) Administrative support: None; (III) Provision of study materials or patients: R Liu, Y Huang, K Chai, T Xiong; (IV) Collection and assembly of data: L Qu, W Zhou; (V) Data analysis and interpretation: Z Jia; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Linlin Qu. Department of Laboratory Medicine, the First Hospital of Jilin University, Changchun, China. Email: qull@jlu.edu.cn; Wei Xia. College of Medical Technology, Beihua University, Jilin, China. Email: xiawei4016@126.com.

Background: Neonatal leukemoid reaction (NLR) is often accompanied by infectious or non-infectious diseases, a low birth weight, sepsis, prematurity, ventricular hemorrhage, and bronchial dysplasia. It has an incidence rate of 1.3–15% and a mortality rate of about 41.4%. Previous studies on NLR have largely focused on its pathogenesis and clinical cases, but little is known about its prognostic laboratory indicators. We found that some of the NLR exhibited obviously elevation in liver function tests like aspartate transaminase (AST) and lactate dehydrogenase (LDH) which were not took by all the LR infants. The necessity for liver function tests for the prognosis of NLR was still unclear.

Methods: A total of 39 premature infants with NLR at the First Hospital of Jilin University between March 2016 and March 2017 were included in this retrospective cohort study. The infants were divided into death and cured group based on the clinical outcomes. Premature infants with LR and death were defined as the case group (n=14), while infants without death were defined as the control group (n=25). Confounding factors such as age and gender between the two groups were controlled. Blood routine tests, including the white blood cell (WBC) count and subtypes, and liver function, and clinical features were recorded and analyzed. T tests were used to examine the differences in the laboratory indicators between the NLR and control groups. Receiver operating characteristic curves (ROCs) and areas under the curve (AUCs) were used to examine laboratory indicators for prognosis.

Results: For predicting clinical outcomes, the ROC curves showed that the cut-off values for AST and LDH were 279 and 1,412 U/L, respectively. The sensitivity and specificity for AST were 92% and 71.43%, respectively, with an AUC of 0.894, while the sensitivity and specificity for LDH were 88% and 78.57%, respectively, with an AUC of 0.911.

Conclusions: This innovative study investigated the NLR prognosis depending on laboratory tests. We found that serum AST and LDH levels had reliable predictive value in determining adverse outcomes of NLR.

Keywords: Neonatal leukemoid reaction; aspartate transaminase (AST); lactate dehydrogenase (LDH); prognosis; laboratory medicine

Submitted Sep 27, 2022. Accepted for publication Dec 07, 2022.
doi: 10.21037/tp-22-543
View this article at: https://dx.doi.org/10.21037/tp-22-543

^ ORCID: 0000-0002-1025-5387.

Introduction

Leukemoid reaction (LR) is a condition that presents with peripheral leukocytosis in hematological diseases and is usually triggered by certain diseases or external stimuli (1). The characteristics of LR include: (I) an elevated white blood cell (WBC) count >50×10^9/L with a "left shift", which occurs in immature granulocytes but no blast or early stage of leukocytes as is often observed in hematological diseases; (II) severe infection, neoplasms (mostly malignant tumors), severe hemorrhage, toxin exposure, such as ethylene glycol, severe burn (2), or exposure to glucocorticoids, in the pathological stimuli of the LR (3); (III) an exclusive diagnosis that can only be decided after the exclusion of hematological diseases, such as myeloproliferative neoplasms, and acute myelocytic leukemia; (IV) quick relief, which usually occurs after the definite reasons for LR have been addressed. Based on the elevated subtypes of leukocytosis, LR is classified into neutrophilia, lymphocytosis, monocytosis, and eosinophilia (4,5).

LR occurs in different populations. In newborn infants, LR is referred to as neonatal leukemoid reaction (NLR), and is often accompanied by infectious or non-infectious diseases, a low birth weight, sepsis, prematurity, intravascular hemolysis, or bronchial dysplasia (6-8). The incidence rate of NLR varies from 1.3% to 15%, and the mortality rate can be as high as 41.4% (1). Previous studies on NLR have largely focused on the pathogenesis of NLR and clinical cases; but little is known about the prognostic laboratory indicators of NLR (7-9). Previously, we found that some of the NLR exhibited obviously elevation in liver function tests, however, which were not tested in all LR infants. Whether liver function tests were necessary? In another hand, as blood collection for serum to test liver function was invasive, whether blood collection for liver function tests was worthy? Pathologically, NLR may induce systemic inflammatory response syndrome (SIRS) and may end with multiple organ dysfunction syndrome (MODS), which can be reflected by enzyme abnormality because of damage in multiple organs like liver, brain and/or heart. Thus, systemic laboratory biomarkers such as aspartate transaminase (AST) and lactate dehydrogenase (LDH) were potentially associated with death in NLR. Therefore, it is necessary to identify prognostic factors among routine laboratory indicators. In this study, we investigated potential prognostic indicators of NLR correlated to the clinical outcomes. We found associations between serum AST and LDH levels and the clinical outcomes of NLR. These factors may help to predict the clinical outcomes of NLR. We present the following article in accordance with the STARD reporting checklist (available at https://tp.amegroups.com/article/view/10.21037/tp-22-543/rc).

Highlight box

Key findings

- The serum AST and LDH levels have reliable predictive value in determining adverse outcomes of NLR.

What is known and what is new?

- Neonatal leukemoid reaction (NLR) is often accompanied by infectious or non-infectious diseases, a low birth weight, sepsis, prematurity, intravascular hemolysis, and bronchial dysplasia, and has an incidence rate of 1.3–15%, and a mortality rate of about 41.4%. Previous studies on NLR have largely focused on its pathogenesis and clinical cases, but little is known about its prognostic laboratory indicators.
- This innovative study investigated the NLR prognosis depending on laboratory tests. We found that serum AST and LDH levels had reliable predictive value in determining adverse outcomes of NLR.

What is the implication, and what should change now?

- In the future, we can use liver function indicators to predict the prognosis of NLR.

Methods

Design overview

This retrospective cohort study was conducted at the First Hospital of Jilin University, Changchun, China. According to the Laboratory Information Management System, premature infants with a WBC count >50×10^9/L were included in the study. According to the outcomes, the NLR patients were divided into the death group and the cured group. The association between liver function and the clinical outcomes were analyzed. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of the First Hospital of Jilin University (No. 2016-458). Individual consent for this retrospective analysis was waived.

Definitions and patient recruitment

Patients' WBCs and differentials were analyzed using the Sysmex XN-9000 Automated Hematology Analyzer. Leukocytosis with a WBC count >50×10^9/L were manually reviewed on blood smears by microscopy. A total of 200 cells were analyzed by the laboratory specialist for each smear. To be diagnosed with NLR, the patients had to meet

the following criteria: (I) be a premature neonatal infant; (II) have a WBC count >50×10^9/L; (III) have no blast or early stage leukocytes; and (IV) have no other hematological diseases.

A total of 39 premature infants hospitalized at the Neonatal Pediatrics Department of the First Hospital of Jilin University between March 2016 and March 2017 were included in the study. And we estimated the sample size: enrollment of 39 patients (14 of NLR with death were case group and 25 of NLR without death were control group) would provide 90% power based on the one-sided alpha of 0.05. The premature babies with LR were defined as case group, while those without LR were defined as control group. Instead of common matching method, we analyzed the difference of important characteristics such as age and gender between the case and control groups, and found no significant difference by *t*-test.

Clinical characteristics

The clinical characteristics included the maternal gestational week, birth weight, gender, sepsis, bronchopulmonary dysplasia, cytomegalovirus (CMV) infection, and pneumonia. The adverse clinical outcomes included sepsis and retinopathy. The clinical outcomes were recorded as clinical improvement or death.

Laboratory analysis

Liver function indicators included serum alanine transaminase (ALT), aspartate transaminase (AST), lactate dehydrogenase (LDH), γ-glutamyl transpeptidase (γ-GT), cholinesterase (CHE), direct bilirubin (DBIL), which were detected using the AU5800 automated analyzer (manufactured by Beckman Coulter. Inc., USA), and the corollary reagents. The high-sensitive C-reactive protein (hs-CRP) levels were quantified using the immunoturbidimetric method on Beckman 5821 (manufactured by Beckman Coulter. Inc., USA). CMV copies were quantified using Roche real-time fluorescence quantitative polymerase chain reaction system.

Statistical methods

The statistical analysis was conducted using IBM SPSS Statistics Software 26.0. Differences among the subgroups in terms of the distributions of liver function indicators, hs-CRP, and CMV were compared using the Chi-square test and Mann-Whitney U non-parametric tests. A 2-tailed P value <0.05 was considered statistically significant. The events of NLR and death were set as the outcome variables. A receiver operating characteristic (ROC) curve analysis was conducted for those laboratory indicators of the events. The areas under the curve (AUC) and the sensitivity were evaluated. To obtain the optimized cut-off value, the distance (d) between the point (0, 1) and any point on the ROC curve was minimized: $\left(\text{Min}\left(\text{d}\right)=\sqrt{\left(1-\text{sensitivity}\right)^2+\left(1-\text{specificity}\right)^2}\right)$. The 95% confidence intervals (CIs) were determined by a bootstrap analysis. Potential confounders were controlled through a stratified analysis and multivariate logistic regressions.

Results

Baseline of the case and control groups

A total of 39 premature infants with NLR were included as a cohort in the study. According to the outcomes, the case group had 14 death cases, and the control group had 25 clinically cured cases. The mean gestational weeks and birth weight of the case and control groups were (28.2±1.1) weeks and (2,021.9±510.1) g and (29.5±1.6) weeks and (1,936.8±378.2) g, respectively. There were no statistically significant differences in mean gestational age and birth weight between the case and control groups (with P values 0.27 and 0.31, respectively). In relation to the clinical outcomes of the case group, 14 (35.9%) infants died and 25 (64.1%) showed clinical improvement. No statistically significant differences were observed between the two groups in terms of gender, fetal growth retardation, retinopathy, or delivery mode (*Table 1*).

Results of the laboratory analysis

The laboratory indicator results are set out in *Table 2*. In relation to the liver function indicators and CRP, the levels of AST and LDH in the case and control group were respectively (372.6±215.7) U/L and (2,240.1±1,831.5) U/L and (44.8±30.0) U/L and (886.4±435.0) U/L, which were higher in case group (both P<0.0001). The serum GGT, CHE, DBIL, and hs-CRP levels did not differ significantly between the 2 groups (P>0.05). The serum AST and LDH levels in the death group were significantly higher than those in the clinical improvement group and the control group, and the difference was statistically significant (P<0.0001) (*Figure 1*). We also examined correlations between the laboratory indicators and clinical outcomes.

Table 1 Basic information of infants in the case and control groups (N=39)

Characteristic	Case group (n=14)	Control group (n=25)	P value
Gestational week (w) mean ± SD	28.2±1.1	29.5±1.6	0.27
Birth weight (g) mean ± SD	2,021.9±510.1	1,936.8±378.2	0.31
Gender (n, %)			
Male	7, 50.0%	13, 52.0%	1.0
Female	7, 50.0%	12, 48.0%	
Sepsis (n, %)	12, 85.7%	7, 28.0%	<0.001*
Bronchopulmonary dysplasia (n, %)	11, 78.6%	2, 12.5%	<0.001*
CMV infection (n, %)	6, 42.9%	8, 32.0%	0.51
Retinopathy (n, %)	1, 7.1%	1, 4.0%	1.0

*, P<0.05. SD, standard deviation; CMV, cytomegalovirus.

Table 2 Serum levels of laboratory indicators between the case and control groups (N=39)

Characteristic	Case group (n=14)	Control group (n=25)	P value
AST (U/L)	372.6±215.7	44.8±30.0	<0.0001*
LDH (U/L)	2,240.1±1,851.5	886.4±435.0	<0.0001*
CRP (mg/L)	61.3±37.4	28.6±9.7	0.821
TBIL (μmol/L)	67.3±23.8	113.4±31.5	0.310
γ-GT (U/L)	95.0±40.5	116.6±18.1	0.274
CHE (U/L)	3,550.7±485.3	3,939.0±321.7	0.687

Data are shown as mean ± SD. *, P<0.05. AST, aspartate transaminase; LDH, lactate dehydrogenase; CRP, C-reactive protein; TBIL, total bilirubin; γ-GT, γ-glutamyl transpeptidase; CHE, cholinesterase; SD, standard deviation.

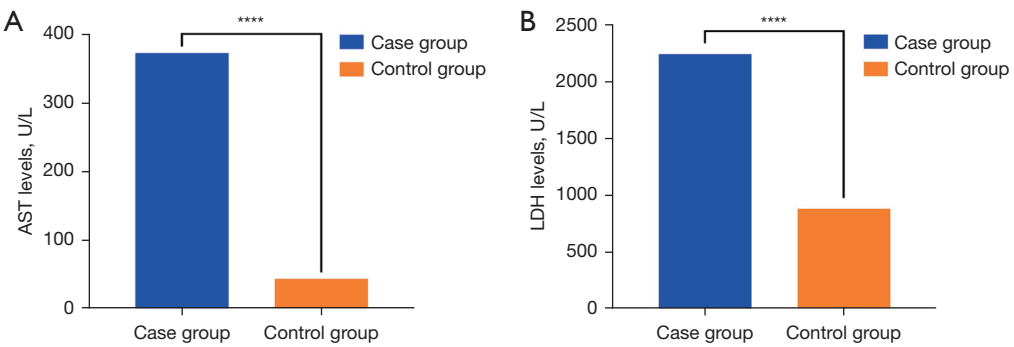

Figure 1 Serum AST and LDH levels in the case (NLR) and control group (****, P<0.0001). The NLR patients were split into the clinical improvement and death groups based on the outcomes of the patients. (A) AST serum levels in different groups. (B) LDH serum levels in different groups. AST, aspartate transaminase; LDH, lactate dehydrogenase; NLR, neonatal leukemoid reaction.

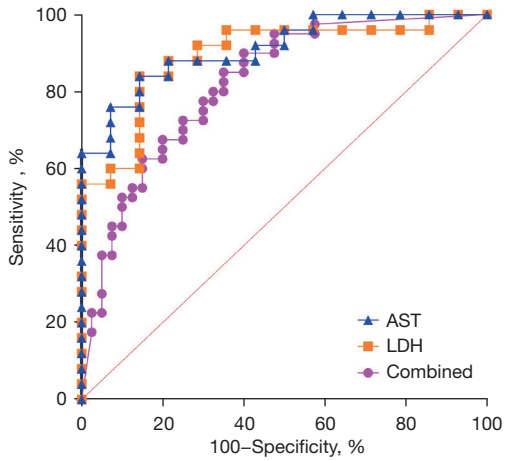

Figure 2 The ROC curves for AST and LDH were plotted based on the levels and clinical outcomes of the NLR and control groups. The X-axis shows the specificity, while the Y-axis shows the sensitivity. ROC curve for AST (in blue). The AUC was 0.894 based on a cut-off value of 279 U/L. ROC curve for LDH (in orange). The AUC was 0.911 based on a cut-off value of 1,412 U/L. Combined ROC curve for AST and LDH (in purple); the AUC was 0.821. ROC, receiver operating characteristic; AST, aspartate transaminase; LDH, lactate dehydrogenase; NLR, neonatal leukemoid reaction; AUC, area under the curve.

Predicting characteristics of AST and LDH

The sensitivity and specificity of serum AST and LDH levels on predicting the clinical outcomes were assessed using the ROC curves and AUCs. The ROC curve analysis showed that the cut-off value for AST was 279 U/L, the AUC was 0.894, and AST had a sensitivity and specificity of 88% and 78.58%, respectively. The ROC curve analysis showed that the cut-off value for LDH was 1,412.0 U/L, the AUC was 0.911, and LDH had a sensitivity and specificity of 88.0% and 78.57%, respectively. When AST and LDH were combined, they had an AUC of 0.821 (*Figure 2*).

Results of AST and LDH binary logistic regression

The results of binary logistic regression showed that AST and LDH predicted the prognosis of neonatal leukemoid reaction (OR =85.30, 95% CI: 5.436, 1,339.46) and (OR =12.92, 95% CI: 0.949, 175.89). For the results of OR value and 95% CI, we considered that there was a large relationship with the small sample size of this study.

Discussion

Necessity of the study

LR is usually a temporary condition secondary to pathological stimuli; however, LR in prenatal newborns sometimes results in severe consequences, such as fetal inflammatory response syndrome, or even death. In recent years, some studies have reported laboratory indicators for the prognosis of NLR (9,10); for example, dysplasia appears to be correlated with a poor prognosis. Notably, interlukin-6 and granulocyte colony-stimulating factor have been identified as independent factors that reflect some of the leukocytic actions that may develop into NLR (9). Futhermore, these parameters may be prognostic indicators for preterm infants and can be used in their clinical management after birth.

Clinical etiology of NLR

Typically, a patient with NLR has a leukocyte count >50×10^9/L. Similar to leukemia, LR can be triggered by concomitant disorders (7). In this study, the infants in the case and control groups had leukocyte counts >50×10^9/L (4,7,8,10,11). The NLR patients included in this study were paired with premature newborns without NLR. Compared to the control group, the NLR group had a higher incidence of concomitant disorders, among which bronchopulmonary dysplasia (30, 71.4%) and sepsis (26, 61.9%) were the infront, which was consistent with the existing literatures (5,10,11). Retinal lesions were not found to be significantly correlated with NLR (P=0.06) (*Table 2*). Morag *et al.* reported that if delayed leukocytosis occurred 72 hours after birth, the incidence rate and pathogenic factors of sepsis increased, such as necrotizing enterocolitis (12).

Prognostic value of AST and LDH

This was the first study to reveal a correlation between liver function parameters and poor clinical outcomes of NLR. During the treatment of NLR, hs-CRP, AST, ALT, γ-GT, CHE, DBIL, IBIL, LDH, and ALB were frequently monitored. Thus, we sought to investigate prognostic value of these frequently used laboratory indicators.

We analyzed differences among these indicators between the case group and the control group. The serum AST, LDH, CRP, and DBIL levels of the case group were higher than those of the control group (P<0.05). Thus, the prognostic value of these 4 indicators were

Table 3 The prediction performance of serum AST and LDH levels

Parameters	Cut-off value (U/L)	AUC	Sensitivity (%)	Specificity (%)	P value
AST	279	0.894	92.00	71.43	<0.0001
LDH	1,412	0.911	88.00	78.57	<0.0001
Combined		0.821	80.00	67.50	<0.0001

AST, aspartate transaminase; LDH, lactate dehydrogenase; AUC, area under the curve.

Table 4 Data validation

Patients	AST	LDH	Clinical prognosis
1	56.3	509	clinical improvement
2	391.9	4,221	death
3	189.9	2,640	clinical improvement
4	23.9	509	clinical improvement
5	341	2,975	death
6	123.6	2,572	clinical improvement
7	66	1,612	clinical improvement
8	33.5	660	clinical improvement
9	47.6	511	clinical improvement
10	231.2	976.1	clinical improvement

Data are shown as the AST and LDH test level (U/L). AST, aspartate transaminase; LDH, lactate dehydrogenase.

analyzed by ROC curves. With a cut-off value of 279 U/L, the sensitivity and specificity of serum AST levels for adverse clinical outcomes were 92% and 71.43% (*Table 3*), respectively, which suggest AST a high level of accuracy in predicting NLR. AST is widely distributed in the heart and, to a lesser extent, the liver, skeletal muscle, and kidneys (13,14), and is often regarded as the most sensitive indicator of liver damage and aids in the diagnosis of myocardial infarction (15). As is often associated with liver damage in patients with clinical sepsis, etiological investigations of NLR have shown that increased serum AST levels were also frequently associated with sepsis (6-8).

In our study, with a cut-off value of 1,412 U/L, the serum LDH levels had a sensitivity and specificity for predicting adverse clinical outcomes of 88% and 78.57% (*Table 3*), respectively. LDH is one of the most important enzymes in the anaerobic metabolism and gluconeogenesis of sugar, catalyzing the reduction and oxidation reactions between propionic acid and L-lactic acid, and the associated alpha-keto acids (16). LDH is widely present in human tissues. It presents in its highest concentrations in the kidneys, followed by cardiac skeletal muscle, and in moderate concentrations in red blood cells (13). Elevations in LDH are often observed in myocardial infarction, liver disease, hematological disorders, skeletal muscle damage, and malignancies (17,18). Thus, LDH levels are associated with disorders that lead to cellular damage and have been shown to reflect severe illness in neonates (18).

LDH levels are of prognostic significance because of the widespread distribution of this enzyme in body tissues and their ability to reflect cellular damage. Studies have examined the use of LDH as an indicator of severe illness in neonates (18). LDH has predictive value in diagnosing perinatal asphyxia (19) and predicting Neonatal Intensive Care Unit stay and the duration of oxygen dependency (20). We observed that LDH was elevated in most infants with LR at the time of disease presentation. To investigate the cause of this and determine the clinical prognosis, we examined whether LDH could be used as a prognostic indicator of NLR.

We also found that the combined AUC of AST and LDH was 0.821. Furthermore, the sensitivity and specificity of AUC of AST and LDH combined for adverse clinical outcomes were 80% and 67.5%, respectively, which suggest that these serum levels combined have a high level of accuracy in terms of their predictive value (P<0.0001).

As the submission of this paper, the study continued to collect 10 cases of neonatal with NLR from January 2018 to September 2022 in the First Hospital of Jilin University for validation (*Table 4*). Two children in the validation group died, with AST and LDH higher than our cut-off value. The diagnosis and medical treatment of neonatal leukemoid reactions have improved greatly in recent years due to the advancement of medical care and diagnosis, the introduction of stratified and graded neonatology, and the establishment of the NICU, resulting in fewer cases of death.

Conclusions

This observational study showed that liver function plays a crucial role in the prognosis of NLR. Among the common indicators, serum AST and LDH levels had obvious correlations with adverse clinical outcomes. Only 39 cases of NLR patients were included in this study, which may be a source of bias; however, our findings indicate that serum AST and LDH levels may be used to predict adverse clinical outcomes in NLR neonates and as possible tools in NLR treatment.

Acknowledgments

Funding: This research was funded by the Natural Science Foundation of Jilin Province (No. 20210101335JC).

Footnote

Reporting Checklist: The authors have completed the STARD reporting checklist. Available at https://tp.amegroups.com/article/view/10.21037/tp-22-543/rc

Data Sharing Statement: Available at https://tp.amegroups.com/article/view/10.21037/tp-22-543/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tp.amegroups.com/article/view/10.21037/tp-22-543/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of The First Hospital of Jilin University (No. 2016-458). Individual consent for this retrospective analysis was waived.

References

1. Bhatia R, Bhatia G. Neonatal leukemoid reaction: a diagnostic dilemna. J Nepal Paediatr Soc 2017;36:298-9.
2. Mandal P, Mukherjee SB. Leukemoid reaction - a tale of 50 years. Indian Pediatr 2015;52:973-4.
3. Mycyk MB, Drendel A, Sigg T, et al. Leukemoid response in ethylene glycol toxication. Vet Hum Toxicol 2002;44:304-6.
4. Al Sbihi AF, Manasrah N, Al Haj FM, et al. A Paraneoplastic Leukemoid Reaction in Primary Lung Sarcoma. Cureus 2021;13:e15047.
5. Chakraborty S, Keenportz B, Woodward S, et al. Paraneoplastic leukemoid reaction in solid tumors. Am J Clin Oncol 2015;38:326-30.
6. Blindar VN, Zubrikhina GN, Sytov AV. Morphological and functional features of peripheral blood neutrophils in cancer patients with sepsis in the early postoperative period (review of literature and results of our own studies). Klin Lab Diagn 2021;66:15-21.
7. Duran R, Ozbek UV, Ciftdemir NA, et al. The relationship between leukemoid reaction and perinatal morbidity, mortality, and chorioamnionitis in low birth weight infants. Int J Infect Dis 2010;14:e998-1001.
8. Hoofien A, Yarden-Bilavski H, Ashkenazi S, et al. Leukemoid reaction in the pediatric population: etiologies, outcome, and implications. Eur J Pediatr 2018;177:1029-36.
9. Nakamura T, Hatanaka D, Kusakari M, et al. Neonatal Leukemoid Reaction with Fetal Inflammatory Response Syndrome Is Associated with Elevated Serum Granulocyte Colony Stimulating Factor and Interleukin-6. Tohoku J Exp Med 2018;244:145-9.
10. Portich JP, Faulhaber GAM. Leukemoid reaction: A 21st-century cohort study. Int J Lab Hematol 2020;42:134-9.
11. Ellison TA, Mandal K. Leukemoid reaction: Case report. J Thorac Cardiovasc Surg 2018;155:e117-8.
12. Morag I, Dunn M, Nayot D, et al. Leukocytosis in very low birth weight neonates: associated clinical factors and neonatal outcomes. J Perinatol 2008;28:680-4.
13. Otto-Ślusarczyk D, Graboń W, Mielczarek-Puta M. Aspartate aminotransferase--key enzyme in the human systemic metabolism. Postepy Hig Med Dosw (Online) 2016;70:219-30.
14. Lorubbio M, Ognibene A, Salvadori B, et al. Macro-

aspartate aminotransferase in a healthy woman. Clin Mol Hepatol 2020;26:378-81.
15. Panteghini M. Aspartate aminotransferase isoenzymes. Clin Biochem 1990;23:311-9.
16. Khan AA, Allemailem KS, Alhumaydhi FA, et al. The Biochemical and Clinical Perspectives of Lactate Dehydrogenase: An Enzyme of Active Metabolism. Endocr Metab Immune Disord Drug Targets 2020;20:855-68.
17. Farhana A, Lappin SL. Biochemistry, Lactate Dehydrogenase 2022. In: StatPearls. Treasure Island (FL): StatPearls Publishing, 2021.
18. Karlsson M, Dung KT, Thi TL, et al. Lactate dehydrogenase as an indicator of severe illness in neonatal intensive care patients: a longitudinal cohort study. Acta Paediatr 2012;101:1225-31.
19. Reddy S, Dutta S, Narang A. Evaluation of lactate dehydrogenase, creatine kinase and hepatic enzymes for the retrospective diagnosis of perinatal asphyxia among sick neonates. Indian Pediatr 2008;45:144-7.
20. Kamath MK, Asha M, Saihari B, et al. Lactate dehydrogenase as a prognosticating tool in predicting NICU stay and Oxygen dependence in meconium stained amniotic fluid neonates. J Clin of Diagn Res 2019;13:SC11-3.

(English Language Editor: L. Huleatt)

Cite this article as: Liu R, Huang Y, Jia Z, Joseph MJ, Chai K, Xiong T, Zhou W, Qu L, Xia W. Elevated serum AST and LDH levels are associated with infant death in premature babies with neonatal leukemoid reaction: a cohort study. Transl Pediatr 2022;11(12):1920-1927. doi: 10.21037/tp-22-543