Pediatric Health, Medicine and Therapeutics

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Analysis of the Levels of CD40L and NGAL in Umbilical Cord Blood of Preterm Infants with Moderate to Severe Bronchopulmonary Dysplasia and Their Clinical Value: A Single-Center Retrospective Study

Weina Li[1], Xiuya Guo[1], Xian He[1], Huanhuan Ma[1], Yan Li[2], Linlin Fu[2], Xuemin Qie[1]

[1]Department of Neonatology, Baoding Maternal and Child Health Care Hospital, Baoding, Hebei, People's Republic of China; [2]Department of Pediatrics, Baoding Maternal and Child Health Care Hospital, Baoding, Hebei, People's Republic of China

Correspondence: Xuemin Qie, Department of Neonatology, Baoding Maternal and Child Health Care Hospital, Baoding, Hebei, People's Republic of China, Email QieXueminxx88@163.com

Pediatric Health, Medicine and Therapeutics downloaded from https://www.dovepress.com/
For personal use only.

Objective: To examine the concentrations of cluster of differentiation CD40 ligand (CD40L) and neutrophil gelatinase-associated lipocalin (NGAL) in preterm infants with moderate to severe bronchopulmonary dysplasia (BPD), as well as to elucidate their clinical implications.

Methods: A cohort of 138 preterm infants admitted to the neonatal intensive care unit between January 2021 and October 2022 were enrolled and divided into two groups: moderate to severe BPD (n=14) and non-BPD controls (n=124). Clinical data were collected. CD40L and NGAL levels in umbilical cord blood were measured by ELISA. Pearson correlation analysis and multivariate logistic regression were performed to identify risk factors and evaluate diagnostic value using ROC curve analysis.

Results: Infants with moderate to severe BPD had lower 1-minute Apgar scores, prolonged mechanical ventilation, and higher prevalence of maternal smoking and intrauterine infection (all $P<0.05$). CD40L and NGAL levels were significantly higher in BPD infants ($P<0.001$). Pearson analysis showed a strong positive correlation between CD40L and NGAL ($r=0.800$, $P<0.001$). Multivariate logistic regression identified maternal smoking (OR=1.092, 95% CI: 1.030–1.158), intrauterine infection (OR=1.136, 95% CI: 1.027–1.256), elevated CD40L (OR=1.138, 95% CI: 1.042–1.242), and NGAL (OR=1.270, 95% CI: 1.063–1.518) as independent risk factors for BPD. ROC analysis confirmed the diagnostic utility of CD40L and NGAL, with combined assessment showing superior predictive performance.

Conclusion: Elevated levels of CD40L and NGAL in umbilical cord blood of preterm infants with moderate to severe BPD suggest that these biomarkers have high diagnostic value for moderate to severe BPD.

Keywords: bronchopulmonary dysplasia, preterm infants, umbilical cord blood, CD40L, NGAL, clinical value

Introduction

Bronchopulmonary Dysplasia (BPD) represents a prevalent chronic pulmonary condition among preterm infants, primarily distinguished by simplified alveolar architecture and retarded pulmonary vascular maturation. These pathological features significantly impact the short-term and long-term prognosis of preterm infants.[1,2] As our understanding of the pathophysiological mechanisms underlying BPD continues to advance, the importance of early preventive strategies has become increasingly evident. These strategies play a crucial role in improving the outcomes of preterm infants.[3] Therefore, identifying biomarkers for the early prediction and management of BPD holds important clinical significance.

Recent research has demonstrated a notable correlation between various biomarkers in umbilical cord blood and the incidence as well as progression of BPD in preterm infants. For example, studies have shown that umbilical cord blood

Received: 17 April 2025
Accepted: 20 August 2025
Published: 8 October 2025

© 2025 Li et al. This work is published and licensed by Dove Medical Press Limited. The full terms of this license are available at https://www.dovepress.com/terms.php and incorporate the Creative Commons Attribution – Non Commercial (unported, v4.0) License (http://creativecommons.org/licenses/by-nc/4.0/). By accessing the work you hereby accept the Terms. Non-commercial uses of the work are permitted without any further permission from Dove Medical Press Limited, provided the work is properly attributed. For permission for commercial use of this work, please see paragraphs 4.2 and 5 of our Terms (https://www.dovepress.com/terms.php).

concentrations of angiopoietin-1 exhibit a significant inverse correlation with BPD risk in preterm infants. Specifically, lower levels of angiopoietin-1 have been shown to increase the likelihood of BPD development, implicating angiopoietin-1 as a potential biomarker for the prediction of BPD risk.[4] Furthermore, a separate study employed high-performance liquid chromatography-mass spectrometry to examine the umbilical cord blood of 205 preterm infants (gestational age ≤ 28 weeks) and 51 term infants. This analysis revealed the presence of 105 adducts, among which 51 known adducts, including small thiols, direct oxidation products, and reactive aldehydes, exhibited elevated levels in cases of BPD. This study revealed the relationship between oxidative stress markers in umbilical cord blood and BPD.[5] These findings provide important evidence for the early identification of BPD risk through umbilical cord blood biomarkers.

CD40 ligand (CD40L) and Neutrophil gelatinase-associated lipocalin (NGAL) are two important inflammation-related molecules.[6,7] CD40L plays a key role in immune regulation and inflammatory responses, and its abnormal expression is associated with inflammatory diseases and immune cell activation.[8,9] NGAL is an acute-phase reactant protein, the levels of which significantly increase during inflammation and tissue injury, and it has been used for the diagnosis and prognosis evaluation of various diseases.[10,11] Oxidative stress and inflammation are the core pathogenic mechanisms of BPD. They activate abnormal inflammatory cascades in immature lung tissues, directly interfering with the normal construction of alveolar-vascular structures, especially during the critical window of lung development. Persistent inflammation further disrupts the normal lung development process.[12] CD40L deficiency, currently classified as an inborn error of immunity affecting both cellular and humoral immunity, is often associated with pulmonary infections and other clinical manifestations.[13] In addition, elevated urinary NGAL levels have been shown to be associated with prolonged hospital stays in preterm infants.[14] High serum NGAL levels at birth in preterm infants have also been shown to possibly contribute to the progression of BPD.[15] However, there are currently few studies on the changes in levels of CD40L and NGAL in the umbilical cord blood of preterm infants with BPD and their clinical value.

This study seeks to characterize the relationship between the concentrations of CD40L and NGAL in umbilical cord blood of preterm infants and the development of moderate to severe BPD, and to analyze their potential value as early predictive markers. This will provide new insights and potential targets for the early diagnosis and intervention of moderate to severe BPD.

Materials and Methods

Study Population

Source of Data

Based on the reference,[16] the incidence rate of moderate to severe BPD in preterm infants born at 28–31 weeks' gestation is estimated to be approximately 7.93%. The error was set to be no more than 5% (ie, the difference between the upper and lower limits of the confidence interval is 10%). In this study, a two-sided test with 1-α=0.9 was selected, and the sample size was determined using the PASS15.0 software, which determined that a total of 99 subjects were needed to ensure the scientific design of the study.

From January 2021 to October 2022, preterm infants diagnosed with moderate to severe BPD and admitted to the neonatal intensive care unit of our hospital were selected as the study participants. This study adhered to the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Baoding Maternal and Child Health Care Hospital (Approval No.: 2023-01-K006). Informed consent was waived due to the anonymized nature of the data.

Inclusion Criteria

(1) Gestational age of 28–31 weeks; (2) Meeting the diagnostic criteria for moderate to severe BPD;[17] (3) Admitted to the neonatal intensive care unit with a hospital stay exceeding 5 days; (4) Exclusively breastfed; (5) Having complete clinical data and follow-up results.

Exclusion Criteria

(1) Presence of complex congenital heart disease; (2) Suffering from severe diseases of the heart, brain, lungs, kidneys, or other organs; (3) History of major surgery; (4) Unplanned discharge, transfer to another department, transfer to another

 https://doi.org/10.2147/PHMT.S535128

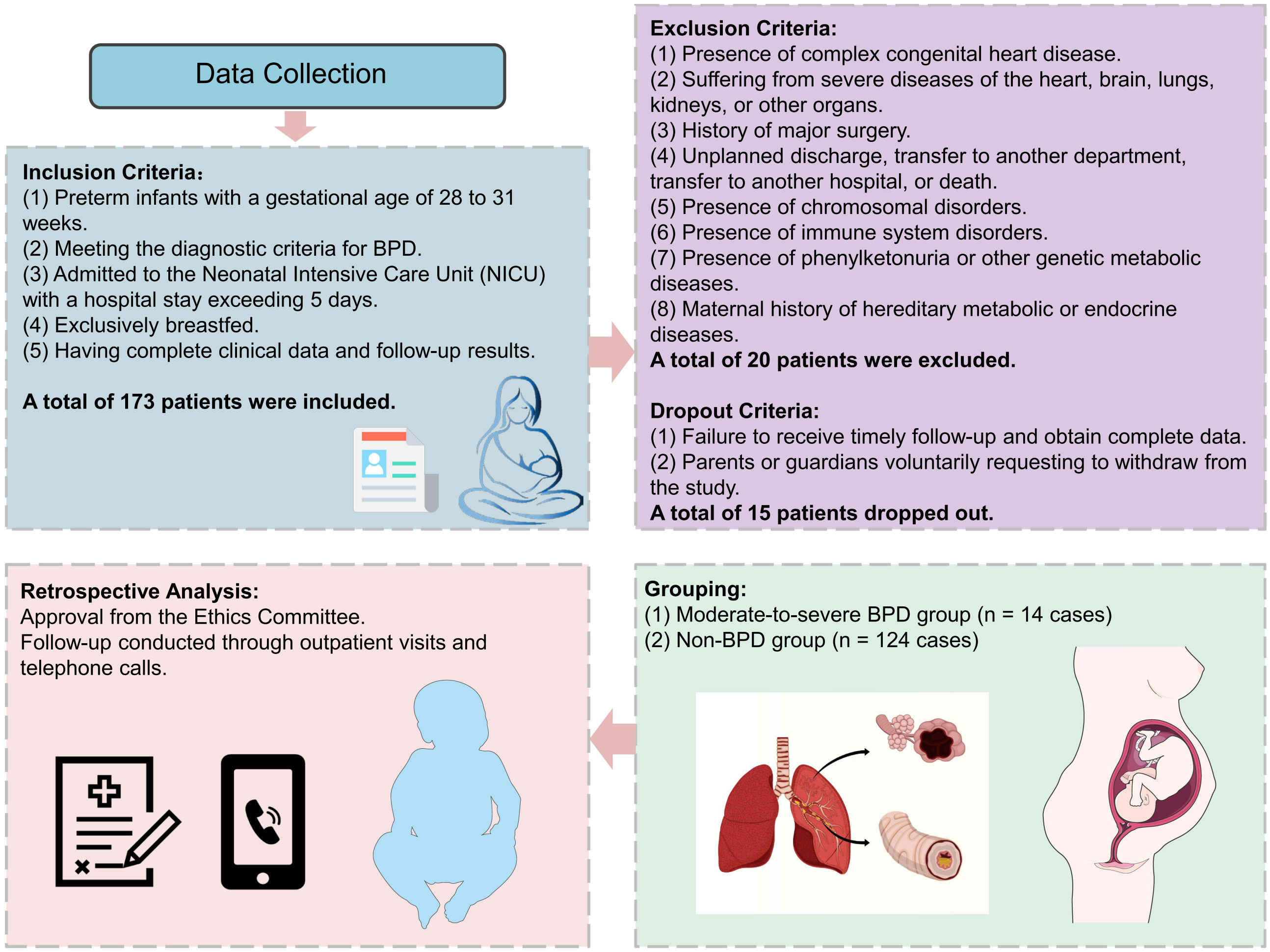

Figure 1 Flowchart of Subject Enrollment.

hospital, or death; (5) Infants with chromosomal diseases; (6) Infants with immune system diseases; (7) Infants with phenylketonuria or other genetic metabolic diseases; (8) Mothers with hereditary metabolic or endocrine diseases.

Dropout Criteria

(1) Failure to complete follow-up and obtain complete data in a timely manner; (2) Parents or guardians voluntarily requesting to withdraw from the study.

In compliance with the predetermined inclusion and exclusion criteria, a cohort of 138 preterm infants was enrolled in this research. These infants were categorized into two distinct groups: the moderate to severe BPD group (n=14) and the non-BPD group (n=124), contingent upon the presence or absence of moderate to severe BPD. A detailed flowchart delineating the subject inclusion process is illustrated in Figure 1.

Methods

Clinical Data Collection

This study employed a retrospective approach to gather clinical data from the enrolled patients, which included the following aspects: (1) Preterm Infant Information: Gestational age (calculated from last menstrual period or early ultrasound), sex, birth weight, delivery mode (vaginal or cesarean section), singleton/multiple birth status, and Apgar scores at 1 and 5 minutes post-delivery. (2) Complications and Treatment of Preterm Infants: Presence of neonatal respiratory distress syndrome (NRDS), patent ductus arteriosus (PDA), neonatal sepsis (NS), and neonatal pneumonia. Use of mechanical ventilation, caffeine, and pulmonary surfactant. Recording of the number of blood transfusions,

 https://doi.org/10.2147/PHMT.S535128

duration of mechanical ventilation, duration of oxygen therapy, and oxygen concentration (<40%, ≥40%). (3) Maternal Information: Age, smoking during pregnancy, premature rupture of membranes, intrauterine infection, pregnancy complications (hypertension, diabetes), and whether corticosteroids were used prenatally.

Specimen Collection and Detection

Umbilical cord blood was obtained from all enrolled infants at birth and was immediately processed by centrifugation.[18] The supernatant was then stored at −80°C in our hospital's biobank for subsequent analysis. The levels of CD40L and NGAL in umbilical cord blood were measured using enzyme-linked immunosorbent assay (ELISA). The ELISA kits were purchased from Wuhan Bailing Biotechnology Co., Ltd., with product numbers HM10346 and HM10120, respectively. The detection procedures were carried out according to the kit instructions.

Statistical Analysis

The data underwent analysis through the utilization of SPSS 26.0 software. Initially, normality tests were executed on the dataset. Normally distributed data are presented as mean ± standard deviation ($\bar{x} \pm s$) and were analyzed using independent samples *t*-tests. Non-normally distributed continuous variables are expressed as median and interquartile range [*M* (*P*25, *P*75)] and were compared using Mann–Whitney *U*-tests. Categorical variables are reported as frequency counts (n) and corresponding percentages (%). Statistical comparisons between groups were performed employing the chi-square (χ^2) test. The correlation between CD40L and NGAL levels in umbilical cord blood was evaluated through Pearson correlation analysis. Logistic regression analysis was utilized to identify risk factors associated with moderate to severe BPD in preterm infants. The diagnostic value of CD40L and NGAL in umbilical cord blood for moderate to severe BPD was evaluated using receiver operating characteristic (ROC) curves. In this study, a *P*-value of less than 0.05 was deemed statistically significant.

Results

Comparison of General Data

Comparative analysis revealed significant differences between the non-BPD and moderate-to-severe BPD groups. Infants with moderate-to-severe BPD demonstrated significantly lower 1-minute Apgar scores ($P<0.05$) and required longer durations of both mechanical ventilation and oxygen therapy ($P<0.05$) compared to non-BPD infants. Other neonatal characteristics showed no statistically significant intergroup differences ($P>0.05$ for all comparisons). Maternal factors analysis indicated significantly higher rates of prenatal smoking exposure ($P<0.05$) and intrauterine infection ($P<0.05$) in the moderate-to-severe BPD group. No other maternal variables reached statistical significance ($P>0.05$). Complete comparative data are presented in Table 1.

Table 1 Comparison of General Data

Variables	Moderate to Severe BPD Group (n=14)	Non-BPD Group (n=124)	χ^2/Z/t	P
Preterm Infant Information				
Gestational Age (weeks)	29.00 (28.00, 30.25)	29.00 (28.00, 30.00)	−0.136^	0.892
Sex [n (%)]			0.154#	0.695
Male	8 (57.14)	64 (51.61)		
Female	6 (42.86)	60 (48.39)		
Birth Weight (g)	1359.50 (1253.75, 1419.25)	1353.00 (1282.50, 1394.50)	−0.264^	0.791
Mode of Delivery [n (%)]			0.162#	0.687
Vaginal	7 (50.00)	69 (55.65)		
Cesarean	7 (50.00)	55 (44.35)		

(*Continued*)

Table 1 (Continued).

Variables	Moderate to Severe BPD Group (n=14)	Non-BPD Group (n=124)	χ^2/Z/t	P
Number of Fetuses			2.144#	0.143
Singleton	7 (50.00)	86 (69.35)		
Multiple	7 (50.00)	38 (30.65)		
1 min Apgar Score	5.00 (3.00, 6.00)	7.00 (5.25, 7.00)	−3.934^	<0.001
5 min Apgar Score	7.00 (6.00, 7.25)	8.00 (7.00, 8.00)	−1.608^	0.108
NRDS [n (%)]	12 (85.71)	102 (82.26)	0.105#	0.746
PDA [n (%)]	5 (35.71)	37 (29.84)	0.205#	0.651
NS [n (%)]	3 (21.43)	17 (13.71)	0.605#	0.437
Neonatal Pneumonia [n (%)]	8 (57.14)	54 (43.55)	0.940#	0.332
Mechanical Ventilation [n (%)]	8 (57.14)	45 (36.29)	2.312#	0.128
Duration of Mechanical Ventilation (days)	28.00 (0.00, 32.50)	0.00 (0.00, 23.00)	−1.978^	0.048
Duration of Oxygen Therapy (days)	30.00 (28.00, 30.00)	23.00 (20.00, 25.00)	−6.144^	<0.001
Oxygen Concentration			0.254#	0.614
<40% [n (%)]	11 (78.57)	104 (83.87)		
≥40% [n (%)]	3 (21.43)	20 (16.13)		
Use of Caffeine [n (%)]	12 (85.71)	103 (83.06)	0.064#	0.801
Use of Pulmonary Surfactant [n (%)]	11 (78.57)	95 (76.61)	0.027#	0.869
Number of Blood Transfusions	1.00 (0.75, 2.00)	1.00 (1.00, 2.00)	−0.964^	0.335
Maternal Information				
Age (years)	28.00 (25.75, 30.00)	29.00 (27.00, 30.00)	−0.985^	0.325
Smoking During Pregnancy [n (%)]	7 (50.00)	17 (13.71)	11.532#	0.001
Premature Rupture of Membranes [n (%)]	3 (21.43)	28 (22.58)	0.010#	0.922
Intrauterine Infection [n (%)]	7 (50.00)	6 (4.84)	30.068#	<0.001
Pregnancy Complications [n (%)]				
Hypertension:	3 (21.43)	20 (16.13)	0.254#	0.614
Diabetes	4 (28.57)	33 (26.61)	0.025#	0.875
Use of Corticosteroids [n (%)]	9 (64.29)	99 (79.84)	1.789#	0.181

Notes: ^represents the *Z* value, and #represents the χ^2 value.
Abbreviations: BPD, bronchopulmonary dysplasia; NRDS, neonatal respiratory distress syndrome; PDA, patent ductus arteriosus; NS, neonatal sepsis.

Comparison of CD40L and NGAL in Umbilical Cord Blood

Umbilical cord blood analysis demonstrated significantly elevated concentrations of both CD40L and NGAL in the moderate-to-severe BPD group compared to non-BPD controls (P<0.001), as shown in Figure 2.

Correlation Analysis of CD40L and NGAL in Umbilical Cord Blood

Pearson correlation analysis showed that the levels of CD40L and NGAL in the umbilical cord blood of preterm infants with moderate to severe BPD were positively correlated (r=0.800, P<0.001), as shown in Figure 3.

Multivariate Logistic Regression Analysis of Risk Factors for Moderate to Severe BPD

A multivariate logistic regression analysis was conducted with maternal smoking during pregnancy, intrauterine infection, and levels of CD40L and NGAL in umbilical cord blood as independent variables, and the occurrence of moderate to severe BPD as the dependent variable (yes=1, no=0). The results showed that maternal smoking during pregnancy (OR=1.092, 95% CI: 1.030–1.158), intrauterine infection (OR=1.136, 95% CI: 1.027–1.256), and elevated levels of CD40L (OR=1.138, 95% CI: 1.042–1.242) and NGAL (OR=1.270, 95% CI: 1.063–1.518) in umbilical cord blood were independent risk factors for the development of moderate to severe BPD. See Table 2.

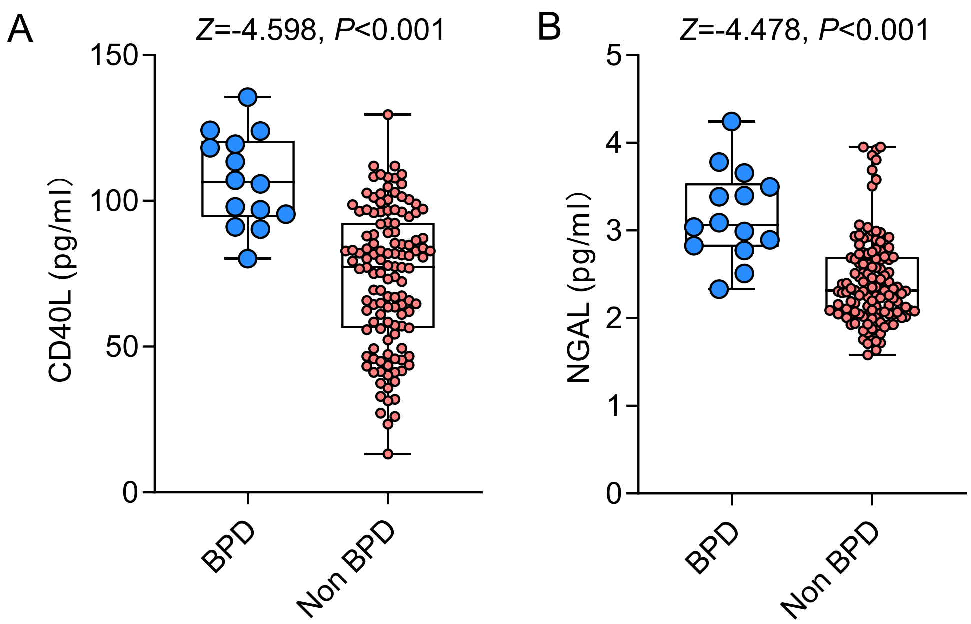

Figure 2 Comparison of CD40L and NGAL in Umbilical Cord Blood.
Notes: (**A**) The expression levels of CD40L in umbilical cord blood from BPD and non-BPD cases; (**B**) The expression levels of NGAL in umbilical cord blood from BPD and non-BPD cases.

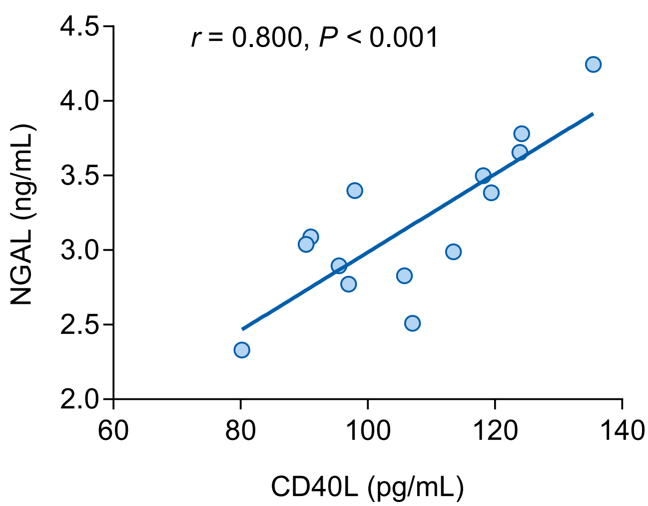

Figure 3 Correlation analysis results of CD40L and NGAL levels in umbilical cord blood.

Diagnostic Value of CD40L and NGAL in Umbilical Cord Blood for Moderate to Severe BPD

ROC curve analysis showed that the AUC values for CD40L, NGAL, and the combined use of CD40L and NGAL in diagnosing moderate to severe BPD were 0.876 (95% CI: 0.796–0.956), 0.866 (95% CI: 0.786–0.946), and 0.933 (95%

Table 2 Multivariate Logistic Regression Analysis of Risk Factors for Moderate to Severe BPD

Index	*β*	*S.E*	*Walds*	*P*	*OR*	95% CI
Maternal Smoking During Pregnancy	0.088	0.030	8.722	0.003	1.092	1.030–1.158
Intrauterine Infection	0.128	0.051	6.182	0.013	1.136	1.027–1.256
CD40L	0.129	0.045	8.367	0.004	1.138	1.042–1.242
NGAL	0.239	0.091	6.918	0.009	1.270	1.063–1.518

Abbreviations: BPD, bronchopulmonary dysplasia; CD40L, CD40 ligand; NGAL, neutrophil gelatinase-associated lipocalin.

Table 3 Diagnostic Value of CD40L and NGAL in Umbilical Cord Blood for Moderate to Severe BPD

Index	Cut-off Value	Sensitivity%	Specificity%	AUC	95% CI
CD40L	89.85	73.39	92.86	0.876	0.796–0.956
NGAL	2.77	80.65	85.71	0.866	0.786–0.946
CD40L+ NGAL	-	84.68	93.86	0.933	0.882–0.985

Abbreviations: BPD, bronchopulmonary dysplasia; CD40L, CD40 ligand; NGAL, neutrophil gelatinase-associated lipocalin.

CI: 0.882–0.985), respectively. The combined diagnosis of CD40L and NGAL had higher sensitivity and specificity compared to the individual markers, as shown in Table 3 and Figure 4.

Discussion

BPD is a chronic pulmonary disorder observed in preterm infants, precipitated by multifactorial contributors such as premature birth, mechanical ventilation, exposure to high concentrations of inhaled oxygen, and infection.[19] Infants with BPD often cannot be weaned off oxygen for a long time after birth, and are prone to symptoms such as dyspnea and recurrent respiratory infections. Severe cases may progress to life-threatening complications including pulmonary hypertension and cardiac failure.[20,21] Consequently, the identification of reliable biomarkers for BPD diagnosis facilitates early intervention strategies, enhances clinical management, and ultimately improves survival outcomes in preterm neonates.

CD40L is a type II transmembrane protein and a member of the tumor necrosis factor (TNF) gene superfamily. It mainly activates B cells, T cells, and dendritic cells through interaction with the CD40 receptor, and promotes humoral and cellular immune responses against tumors.[22–24] Other studies have also shown that inhibiting the CD40L/CD40 pathway can significantly reduce transfusion-related acute lung injury and suppress pulmonary inflammatory responses.[25] A previous research showed that patients with CD40L deficiency often exhibit both cellular and humoral immune deficiencies and frequently suffer from pulmonary infections.[13] Sitaru et al reported elevated levels of CD40L in umbilical cord platelets in cases of chorioamnionitis, suggesting that CD40L may play a significant role in inflammation associated with intrauterine infection.[26] The findings of this study demonstrate significantly elevated CD40L

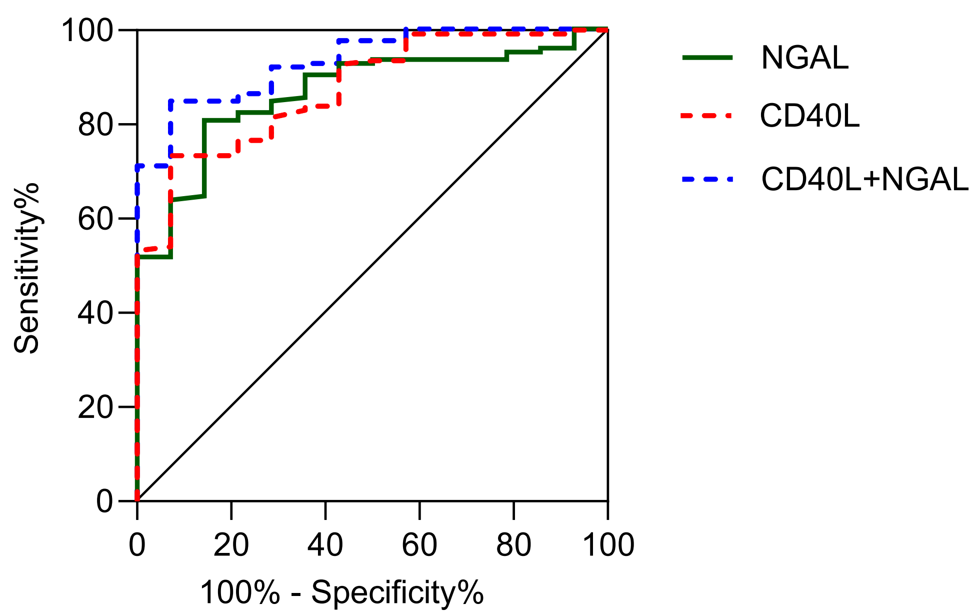

Figure 4 ROC curves of CD40L and NGAL in umbilical cord blood for diagnosing moderate to severe BPD.

concentrations in umbilical cord blood from infants with moderate-to-severe BPD, indicating a potential pathophysiological role of CD40L in both the initiation and progression of bronchopulmonary dysplasia. The possible reason is that CD40L enhances immune responses by secreting a large number of inflammatory factors, such as IL-1β, IL-6, TNF-α, etc., which exacerbate chronic pulmonary inflammation and tissue damage.[22]

NGAL, a member of the lipocalin superfamily, was originally identified in neutrophils; however, its expression is notably upregulated in the kidneys, liver, and epithelial cells under diverse pathological states.[27,28] Studies have also shown that NGAL levels increase in various inflammatory diseases, and its changes are related to disease severity and prognosis.[28–30] Kocaoğlu et al found that NGAL levels in bronchoalveolar lavage fluid and serum significantly increased under mechanical ventilation treatment, and were associated with the degree of lung injury in patients.[31] In this study, we observed a marked elevation in the concentration of NGAL within umbilical cord blood of preterm infants exhibiting moderate to severe BPD, suggesting a potential role for NGAL in the pathogenesis of BPD. Multivariate logistic regression analysis showed that the levels of CD40L (OR=1.138, 95% CI: 1.042–1.242) and NGAL (OR=1.270, 95% CI: 1.063–1.518) in umbilical cord blood were risk factors for the occurrence of moderate to severe BPD, and their elevated levels may reflect the inflammatory state of BPD, further supporting their potential as indicators for BPD risk assessment.

Pearson correlation analysis showed that the levels of CD40L and NGAL in the umbilical cord blood of preterm infants with moderate to severe BPD were positively correlated, suggesting that CD40L and NGAL may have a synergistic effect in the inflammatory response of BPD. The reason may be that CD40L activates the CD40 signaling pathway to promote the release of inflammatory factors, while NGAL further amplifies the inflammatory signal in the inflammatory response. Studies have shown that maternal smoking during pregnancy and intrauterine infection both increase the risk of BPD.[32–34] We further verified this association and found that maternal smoking during pregnancy (OR=1.092, 95% CI: 1.030–1.158) and intrauterine infection (OR=1.136, 95% CI: 1.027–1.256) were important risk factors for the occurrence of moderate to severe BPD. These findings further emphasize the importance of prenatal health management, especially in preventing intrauterine infections and reducing smoking behavior, to reduce the risk of moderate to severe BPD.

ROC curve analysis revealed that the AUC of combined detection of CD40L and NGAL was significantly higher than that of single indicator detection. Moreover, the combined detection of CD40L and NGAL exhibited higher sensitivity and specificity compared to individual indicators. This indicates that the combined detection of CD40L and NGAL holds greater clinical value in the early assessment of BPD. The AUC of combined detection in this study was close to 0.933, indicating that combined detection may more effectively identify preterm infants at higher risk of developing BPD. This could assist clinicians in early assessment and intervention, potentially improving outcomes for preterm infants and reducing the incidence of BPD-related complications.

The present study has several limitations. Firstly, the limited sample size may affect the generalizability and representativeness of the results. Secondly, there may be confounding factors that were not identified or adequately controlled for in the actual study. Thirdly, the dynamic changes of CD40L and NGAL during the progression of BPD were not analyzed. Future studies should consider expanding the sample size and employing more sophisticated methods to assess and control for confounding factors, such as propensity score matching or instrumental variable analysis. Additionally, sampling at multiple time points postpartum is needed to elucidate the dynamic changes of CD40L and NGAL during BPD progression. This would provide a more comprehensive scientific basis for the prevention and treatment of BPD.

Conclusion

The findings suggest that elevated umbilical cord blood concentrations of CD40L and NGAL may serve as potential biomarkers for assessing the risk of moderate-to-severe BPD development in preterm infants. The combined measurement of CD40L and NGAL may offer some value in evaluating the likelihood of moderate-to-severe BPD. Further rigorous studies are warranted to confirm their clinical utility and to explore their potential roles in the management of BPD.

 https://doi.org/10.2147/PHMT.S535128

Data Sharing Statement

The datasets used and/or analyzed in the current study are available from the corresponding author upon reasonable request.

Ethics Statement

This study adhered to the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Baoding Maternal and Child Health Care Hospital (Approval No.: 2023-01-K006). Informed consent was waived due to the anonymized nature of the data.

Acknowledgments

All authors would like to thank all collaborators of this study.

Funding

This study was supported by the S&T Program of Baoding (No. 2341ZF120).

Disclosure

The authors report no conflicts of interest in this work.

References

1. Parsons A, Netsanet A, Seedorf G, Abman SH, Taglauer ES. Understanding the role of placental pathophysiology in the development of bronchopulmonary dysplasia. *Am J Physiol Lung Cell Mol Physiol*. 2022;323(6):L651–L658. doi:10.1152/ajplung.00204.2022
2. Zhou YZ, Wang T, Fu XM, Peng BM, Fu Z. Prognosis of bronchopulmonary dysplasia. *Zhongguo Dang Dai Er Ke Za Zhi*. 2025;27(1):115–120. doi:10.7499/j.issn.1008-8830.2406004
3. Dini G, Ceccarelli S, Celi F. Strategies for the prevention of bronchopulmonary dysplasia. *Front Pediatr*. 2024;12:1439265. doi:10.3389/fped.2024.1439265
4. Yang J, Wang Y, Wu Y, et al. Association of cord blood Ang-1 and sCD105 levels with bronchopulmonary dysplasia in preterm infants. *BMC Pediatr*. 2024;24(1):451. doi:10.1186/s12887-024-04932-7
5. Lin ET, Bae Y, Birkett R, et al. Cord blood adductomics reveals oxidative stress exposure pathways of Bronchopulmonary Dysplasia. *Antioxidants*. 2024;13(4):494. doi:10.3390/antiox13040494
6. Strohm L, Daiber A, Ubbens H, et al. Role of inflammatory signaling pathways involving the CD40-CD40L-TRAF cascade in diabetes and hypertension-insights from animal and human studies. *Basic Res Cardiol*. 2024;119(4):1–18. doi:10.1007/s00395-024-01045-1
7. Gumpper-Fedus K, Chasser K, Pita-Grisanti V, et al. Systemic neutrophil gelatinase-associated lipocalin alterations in chronic pancreatitis: a multicenter, cross-sectional study. *Clin Transl Gastroenterol*. 2024;15(4):e00686. doi:10.14309/ctg.0000000000000686
8. Sharifi A, Vahedi H, Honarvar MR, et al. Vitamin D decreases CD40L gene expression in ulcerative colitis patients: a randomized, double-blinded, placebo-controlled trial. *Turk J Gastroenterol*. 2020;31(2):99–104. doi:10.5152/tjg.2020.181028
9. Choi H, Lee HJ, Sohn HJ, Kim TG. CD40 ligand stimulation affects the number and memory phenotypes of human peripheral CD8(+) T cells. *BMC Immunol*. 2023;24(1):15. doi:10.1186/s12865-023-00547-2
10. Lin TY, Leu HB, Wu YW, et al. Prognostic utility of neutrophil gelatinase-associated lipocalin (NGAL) levels for cardiovascular events in patients with stable coronary artery disease treated with percutaneous coronary intervention: a prospective longitudinal cohort study. *Biomark Res*. 2025;13(1):24. doi:10.1186/s40364-025-00737-7
11. Laurberg M, Saegerman C, Jacobsen S, et al. Use of admission serum neutrophil gelatinase-associated lipocalin (NGAL) concentrations as a marker of sepsis and outcome in neonatal foals. *PLoS One*. 2023;18(5):e0285819. doi:10.1371/journal.pone.0285819
12. Holzfurtner L, Shahzad T, Dong Y, et al. When inflammation meets lung development—an update on the pathogenesis of bronchopulmonary dysplasia. *Mol Cell Pediatr*. 2022;9(1):7. doi:10.1186/s40348-022-00137-z
13. Leite LFB, Máximo TA, Mosca T, Forte WCN. CD40 ligand deficiency. *Allergol Immunopathol*. 2020;48(4):409–413. doi:10.1016/j.aller.2019.08.005
14. Silva Barbosa JD, Meneses GC, Castelo LR, et al. Urinary cystatin-C and urinary NGAL associated with sepsis predicts longer hospital stay in premature newborns. *Biomarker Med*. 2024;18(15–16):649–658. doi:10.1080/17520363.2024.2377532
15. Inoue H, Ohga S, Kusuda T, et al. Serum neutrophil gelatinase-associated lipocalin as a predictor of the development of bronchopulmonary dysplasia in preterm infants. *Early Hum Dev*. 2013;89(6):425–429. doi:10.1016/j.earlhumdev.2012.12.011
16. Dou C, Yu YH, Zhuo QC, et al. Longer duration of initial invasive mechanical ventilation is still a crucial risk factor for moderate-to-severe bronchopulmonary dysplasia in very preterm infants: a multicenter prospective study. *World J Pediatr*. 2023;19(6):577–585. doi:10.1007/s12519-022-00671-w
17. Sahni M, Mowes AK. Bronchopulmonary Dysplasia. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing LLC; 2025.
18. Waller-Wise R. Umbilical Cord Blood Banking: an Update For Childbirth Educators. *J Perinat Educ*. 2022;31(4):199–205. doi:10.1891/JPE-2021-0006
19. Kostekci YE, Bakırarar B, Okulu E, Erdeve O, Atasay B, Arsan S. An early prediction model for estimating bronchopulmonary dysplasia in preterm infants. *Neonatology*. 2023;120(6):709–717. doi:10.1159/000533299

20. El-Saie A, Varghese NP, Webb MK, et al. Bronchopulmonary dysplasia - associated pulmonary hypertension: an updated review. *Semin Perinatol*. 2023;47(6):151817. doi:10.1016/j.semperi.2023.151817
21. Chaw PS, Hua L, Cunningham S, Campbell H, Mikolajczyk R, Nair H. Respiratory syncytial virus-associated acute lower respiratory infections in children with bronchopulmonary dysplasia: systematic review and meta-analysis. *J Infect Dis*. 2020;222(Suppl 7):S620–S627. doi:10.1093/infdis/jiz492
22. Tang T, Cheng X, Truong B, Sun L, Yang X, Wang H. Molecular basis and therapeutic implications of CD40/CD40L immune checkpoint. *Pharmacol Ther*. 2021;219:107709. doi:10.1016/j.pharmthera.2020.107709
23. Laman JD, Claassen E, Noelle RJ. Functions of CD40 and Its Ligand, gp39 (CD40L). *Crit Rev Immunol*. 2017;37(2–6):371–420. doi:10.1615/CritRevImmunol.v37.i2-6.100
24. Chand Dakal T, Dhabhai B, Agarwal D, et al. Mechanistic basis of co-stimulatory CD40-CD40L ligation mediated regulation of immune responses in cancer and autoimmune disorders. *Immunobiology*. 2020;225(2):151899. doi:10.1016/j.imbio.2019.151899
25. Tariket S, Hamzeh-Cognasse H, Laradi S, et al. Evidence of CD40L/CD40 pathway involvement in experimental transfusion-related acute lung injury. *Sci Rep*. 2019;9(1):12536. doi:10.1038/s41598-019-49040-0
26. Sitaru AG, Speer CP, Holzhauer S, Obergfell A, Walter U, Grossmann R. Chorioamnionitis is associated with increased CD40L expression on cord blood platelets. *Thromb Haemost*. 2005;94(6):1219–1223. doi:10.1160/TH05-02-0127
27. Romejko K, Markowska M, Niemczyk S. The review of current knowledge on Neutrophil Gelatinase-Associated Lipocalin (NGAL). *Int J Mol Sci*. 2023;24(13):10470. doi:10.3390/ijms241310470
28. Marakala V. Neutrophil gelatinase-associated lipocalin (NGAL) in kidney injury—a systematic review. *Clin Chim Acta*. 2022;536:135–141. doi:10.1016/j.cca.2022.08.029
29. Kardas Yildiz A, Urganci N, Usta AM. Evaluation of fecal neutrophil gelatinase-associated lipocalin levels in childhood inflammatory bowel disease. *J Pediatr Gastroenterol Nutr*. 2025;80:792–798. doi:10.1002/jpn3.70015
30. Chen XR, Wang DX. Serum MCP-1 and NGAL play an important role in the acute inflammatory event of chronic obstructive pulmonary disease. *COPD*. 2021;18(4):425–431. doi:10.1080/15412555.2021.1954151
31. Kocaoğlu Ç. The utility of neutrophil gelatinase-associated lipocalin in the detection of emerging lung injury due to mechanical ventilation in children: a preliminary study. *Turk Arch Pediatr*. 2022;57(1):32–37. doi:10.5152/TurkArchPediatr.2022.21160
32. González-Luis GE, van Westering-Kroon E, Villamor-Martinez E, et al. Tobacco smoking during pregnancy is associated with increased risk of moderate/severe bronchopulmonary dysplasia: a systematic review and meta-analysis. *Front Pediatr*. 2020;8:160. doi:10.3389/fped.2020.00160
33. Villamor-Martinez E, Álvarez-Fuente M, Ghazi AMT, et al. Association of chorioamnionitis with bronchopulmonary dysplasia among preterm infants: a systematic review, meta-analysis, and metaregression. *JAMA Network Open*. 2019;2(11):e1914611. doi:10.1001/jamanetworkopen.2019.14611
34. Yu H, Li D, Zhao X, Fu J. Fetal origin of bronchopulmonary dysplasia: contribution of intrauterine inflammation. *Mol Med*. 2024;30(1):135. doi:10.1186/s10020-024-00909-5

Pediatric Health, Medicine and Therapeutics

Dovepress
Taylor & Francis Group

Publish your work in this journal

Pediatric Health, Medicine and Therapeutics is an international, peer-reviewed, open access journal publishing original research, reports, editorials, reviews and commentaries. All aspects of health maintenance, preventative measures and disease treatment interventions are addressed within the journal. Practitioners from all disciplines are invited to submit their work as well as healthcare researchers and patient support groups. The manuscript management system is completely online and includes a very quick and fair peer-review system. Visit http://www.dovepress.com/testimonials.php to read real quotes from published authors.

Submit your manuscript here: http://www.dovepress.com/pediatric-health-medicine-and-therapeutics-journal