International Journal of General Medicine

Dovepress
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ORIGINAL RESEARCH

Analysis of Risk Factors for Severe Pneumonia Progression in Chlamydia psittaci Infections: A Retrospective Study

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Introduction: Psittacosis pneumonia, caused by *Chlamydia psittaci*, is a zoonotic infection with a severe-case mortality rate of 15–20%. This study aimed to identify risk factors for severe pneumonia and evaluate the discriminative performance of corresponding predictive models.

Methods: In this retrospective study, 51 patients with metagenomic next-generation sequencing (mNGS)-confirmed psittacosis pneumonia were classified into severe (n=20) and non-severe (n=31) groups. Demographic characteristics, clinical manifestations, laboratory parameters, and imaging features were collected. Variables were analyzed using univariate screening, variance inflation factor (VIF)-based multicollinearity control, least absolute shrinkage and selection operator (LASSO) regression, and Firth-penalized logistic regression. Receiver operating characteristic (ROC) analysis evaluated predictive performance.

Results: Patients with severe pneumonia were significantly older ($p = 0.043$) and showed a higher prevalence of underlying diseases ($p = 0.025$) and cardiovascular diseases (CVD, $p = 0.028$). They also exhibited persistent lymphocytopenia, progressive decreases in hemoglobin (Hb) levels, and a higher rate of bilateral lung involvement. LASSO regression identified four key predictors: history of CVD, first lymphocyte count (LYM), second Hb measurement, and lactate dehydrogenase (LDH) level. Firth-penalized logistic regression confirmed that a history of CVD (OR = 4.874, 95% CI: 1.270–22.763) and a decreased second Hb measurement (OR = 0.415, 95% CI: 0.169–0.844) were independent risk factors for severe pneumonia. ROC analysis demonstrated that the combination of CVD history and the second Hb measurement achieved a specificity of 90.32%, while the combination of CVD history and LDH exhibited a sensitivity of 90%. The final multivariable model showed good discriminatory performance, with an area under the curve (AUC) of 0.885, sensitivity of 75%, and specificity of 93.50%.

Conclusion: CVD history and progressive Hb decrease are independent risk factors for severe psittacosis pneumonia. Dynamic monitoring of LYM, Hb, LDH, and CVD history facilitates early risk stratification. The multivariate model demonstrates high predictive accuracy and clinical utility.

Keywords: *Chlamydia psittaci*, severe pneumonia, clinical biomarkers, metagenomic next-generation sequencing, risk factors

Introduction

Psittacosis pneumonia, caused by *Chlamydia psittaci*, is a zoonotic respiratory disease, and humans are universally susceptible to it. The globally reported cases indicate a wide range of hosts, primarily encompassing birds, poultry, and mammals, especially parrots and pigeons.[1] Human transmission occurs mainly through direct contact with infected birds or inhalation of aerosolized particles from contaminated feathers and excreta.[1] Although human-to-human transmission remains rare, sporadic cases have been documented.[2,3] The clinical manifestations exhibit significant heterogeneity, ranging from asymptomatic presentations to severe complications (such as respiratory failure and septic shock). Untreated severe cases demonstrate a case fatality rate of 15%-20%,[4] highlighting its life-threatening potential.The epidemiological surveillance report from the Early Warning and Response System of the European Union (EWRS) in

Received: 6 June 2025
Accepted: 9 September 2025
Published: 18 September 2025

February 2024 stated that there was an increase in psittacosis cases in five countries (Austria, Denmark, Germany, Sweden, and the Netherlands) during the early 2023–2024 period.[5] Global studies have indicated that *Chlamydia psittaci* infection accounts for 1.03% to 7.50% of community-acquired pneumonia (CAP) cases,[6,7] suggesting its clinical burden has been underestimated for a long time. In recent years, the application of metagenomic next-generation sequencing (mNGS) technology has significantly improved the diagnostic accuracy of psittacosis. Specifically, by achieving non-targeted detection of pathogenic nucleic acids, this technology overcomes the limitations of traditional culture methods (time-consuming), serological tests (high cross-reactivity), and polymerase chain reaction (PCR) (insufficient sensitivity), providing an innovative tool for rapid and precise diagnosis. Existing studies have predominantly focused on descriptive clinical analyses, with limited quantitative assessment of risk factors. Therefore, we hypothesized that specific clinical, laboratory, and imaging parameters can predict the progression to severe pneumonia in patients with *Chlamydia psittaci* infection. The primary objective of this retrospective study is to identify these risk factors by analyzing clinical data from 51 mNGS-confirmed cases, thereby providing evidence-based guidance for early clinical intervention and improving patient outcomes.

Materials and Methods

Data Sources

Adult patients with mNGS-confirmed psittacosis pneumonia who were admitted to the Affiliated Jinhua Hospital, Zhejiang University School of Medicine between 2020 and 2024 were retrospectively enrolled. The inclusion criteria were: (1) confirmed diagnosis according to the Chinese Guidelines for the Diagnosis and Treatment of Adult Community-Acquired Pneumonia (2016 version);[8] (2) detection of *Chlamydia psittaci* sequences via mNGS in bronchoalveolar lavage fluid (BALF); (3) hospitalization for treatment; and (4) age ≥ 18 years. The exclusion criteria were: (1) patients with confirmed active *Mycobacterium tuberculosis* infection, invasive fungal infections, or respiratory viral infections by any diagnostic method (including mNGS), or patients detected with pneumonia-associated bacterial pathogens via blood culture; (2) patients with incomplete electronic medical records (EMR).

Patients' clinical data (including demographic characteristics, symptoms, laboratory results, and imaging results) were retrieved through the hospital EMR system. Symptoms were primarily documented as patient-reported chief complaints. For laboratory parameters, complete blood count (CBC) components [white blood cell count (WBC), lymphocyte count (LYM), hemoglobin (Hb), platelet count (PLT), C-reactive protein (CRP), and neutrophil count (NEU)] were collected from two consecutive post-admission measurements, while other biochemical markers were obtained from initial admission values. Imaging analysis was conducted based on the first chest computed tomography (CT) scan obtained during hospitalization. Missing data in continuous variables (eg, LYM) were addressed through multiple imputation techniques.

Pathogenic Examinations

BALF specimens were obtained via bronchoscopy and transported under cryopreservation to certified diagnostic laboratories [including DIAN Diagnostics (Hangzhou, China) and WillingMed Technology (Hangzhou, China)] for pathogen mNGS analysis. All contracted laboratories maintained accreditation status with quality-controlled protocols, ensuring reliable detection performance (ISO 15189).

Diagnostic Criteria

Regarding the definition of severe pneumonia, if one of the following major criteria or three of the minor criteria were met, severe pneumonia was diagnosed. Specifically, the major criteria were: (1) requirement of mechanical ventilation with tracheal intubation; and (2) requirement of vasoactive drug therapy for septic shock after active fluid resuscitation. The minor criteria were: (1) respiratory rate ≥ 30 times/min; (2) oxygenation index (PaO_2/FiO_2) ≤ 250 mmHg; (3) multiple lung lobe infiltration; (4) disturbance of consciousness and/or disorientation; (5) blood urea nitrogen (BUN) ≥ 7.14 mmol/L; (6) systolic blood pressure < 90mmHg and requirement of active fluid resuscitation.[8]

Statistical Analysis

Data management and statistical analyses were performed using R software (v4.3.1). Parameters with > 50% missing rates [eg, B-type natriuretic peptide (BNP)] were excluded from the analysis to ensure data reliability. Normally distributed continuous variables were expressed as mean ± standard deviation and compared using Student's *t*-test. Non-normally distributed continuous variables were summarized as median (interquartile range) and analyzed utilizing the Mann–Whitney *U*-test. Categorical variables were described as frequencies (percentages), with comparisons between groups conducted via χ^2 test or Fisher's exact probability test as appropriate. All continuous variables were standardized using Z-score normalization to mitigate the impact of scale differences.Following univariable analysis, the variance inflation factor (VIF) was calculated for each significant variable. Variables exhibiting a VIF>5 were assessed to determine their independent clinical relevance; redundant indicators were removed, retaining only those with low multicollinearity. We then applied least absolute shrinkage and selection operator (LASSO) logistic regression (α=1) to the remaining variables, using five-fold cross-validation to select the optimal penalty parameter (λ_min) and identify the most informative predictors. Finally, a Firth-penalized logistic regression model was fitted with the LASSO-selected variables to mitigate estimation bias due to the small sample size. Receiver operating characteristic (ROC) curve analysis was employed to evaluate the predictive performance of biomarkers for severe pneumonia progression. The optimal cut-off values were determined by maximizing the Youden index. According to Hosmer et al (2013) and Mandrekar (2010),[9,10] an area under the curve (AUC) greater than 0.7 was considered to indicate acceptable discriminatory ability. A two-tailed α level of 0.05 was deemed statistically significant.

Results

Demographic Characteristics

All cases (n = 51; 28 males and 23 females) were aged 30–83 years (60.61 ± 10.68). In short, 12 patients reported a definitive poultry exposure history. Although 39 patients had no direct contact with poultry, 2 of them had contact with waste/recyclable materials. According to the classification criteria, cases were stratified into severe pneumonia (n = 20) and non-severe groups (n = 31). Three deaths occurred in the severe pneumonia group (case fatality rate: 5.88%). Compared with the non-severe group, the severe pneumonia group demonstrated significantly higher mean age (p = 0.043), as well as the prevalence of underlying comorbidities (p = 0.025) and cardiovascular diseases (CVD) (p = 0.028). In contrast, no statistically significant differences were observed in gender distribution, poultry exposure history, seasonal onset patterns, chief complaints, or clinical outcomes between the two groups (all $p > 0.05$). Detailed results are presented in Table 1.

Laboratory Findings

As shown in Table 2, the median levels of LYM and albumin (ALB) at admission were below normal reference ranges in both groups, with the severe pneumonia group showing significantly lower LYM and ALB values than the non-severe group (p = 0.002 and p = 0.007, respectively). In contrast, compared with the non-severe group, the severe pneumonia group exhibited significantly elevated levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), and D-dimer (DD) (p = 0.015, $p < 0.001$, $p < 0.001$, and p = 0.003, respectively). Although Hb levels differed significantly between the two groups (p = 0.031), the median values in both groups remained within normal limits.

Longitudinal analysis results revealed that the severe pneumonia group maintained significantly lower LYM than the non-severe group during two consecutive post-admission measurements (p = 0.002 and p = 0.039, respectively), with persistently subnormal LYM levels during hospitalization. Although the initial Hb median in both groups was within the normal range, the severe pneumonia group demonstrated markedly reduced Hb levels compared to the non-severe group (p = 0.031). Notably, Hb levels in the severe group declined below the lower limit of normal during the second measurement. Additionally, other parameters (including WBC, PLT, CRP, and NEU) showed no significant intergroup differences in either measurement. Detailed longitudinal profiles are presented in Table 3.

Table 1 Demographics and Clinical Characteristics of 51 Patients with Chlamydia Psittaci Pneumonia

	All (N=51)	Severe (N=20)	Non-severe (N=31)	t/χ^2	p value
Age ($\bar{X} \pm SD$)	60.61±10.68	64.35±9.78	58.19±10.68	t=−2.076	0.043
Exposure to poultry[n (%)]	12(23.53%)	8(40.00%)	4(12.90%)	χ^2=3.569	0.059
Gender[n (%)]					
Male	28(54.90%)	12(60.00%)	16(51.61%)	χ^2=0.345	0.557
Female	23(45.10%)	8(40.00%)	15(48.39%)		
No underlying comorbidities	14(27.45%)	2(10.00%)	12(38.71%)	χ^2=5.031	0.025
Underlying comorbidities[n (%)]					
Cardiovascular Diseases	21(41.18%)	12(60.00%)	9(29.03%)	χ^2=4.813	0.028
Hepatic Diseases	11(21.57%)	6(30.00%)	5(16.13%)	χ^2=0.684	0.408
Endocrine Disorders	5(9.80%)	3(15.00%)	2(6.45%)	χ^2=0.270	0.603
Gastrointestinal (GI) Diseases	3(5.88%)	0(0.00%)	3(9.68%)	χ^2=0.680	0.410
Symptoms[n (%)]					
Fever	50(98.04%)	20(100.00%)	30(96.77%)	**	1
Cough	27(52.94%)	12(60.00%)	15(48.39%)	χ^2=0.658	0.417
Fatigue	19(37.25%)	9(45.00%)	10(32.26%)	χ^2=0.844	0.358
Myalgia	6(11.76%)	0(0.00%)	6(19.35%)	χ^2=2.721	0.099
Headache	5(9.80%)	0(0.00%)	5(16.13%)	χ^2=1.985	0.159
Diarrhea	4(7.84%)	2(10.00%)	2(6.45%)	χ^2=0.000	1
Season of onset[n (%)]					
Autumn or Winter	30(58.82%)	15(75.00%)	15(48.39%)	χ^2=3.555	0.059
Spring or Summer	21(41.18%)	5(25.00%)	16(51.61%)		
Clinical Outcomes[n (%)]					
Improvement	48(94.12%)	17(85.00%)	31(100.00%)	χ^2=2.603	0.107
Mortality	3(5.88%)	3(15.00%)	0(0.00%)		

Note:**Fisher's exact probability test.

Table 2 Initial Post-Admission Laboratory Findings of 51 Patients with Chlamydia Psittaci Pneumonia

		Normal Reference Range	All (N=51)	Severe (N=20)	Non-severe (N=31)	Z	p value
CBC and Inflammatory Markers[M(Q1,Q3)]	WBC($\times10^9$/L)	3.50–9.50	7.61 (6.15, 9.70)	8.26 (6.87, 10.25)	7.56 (5.65, 9.09)	−1.023	0.307
	NEU($\times10^9$/L)	1.80–6.30	6.56 (5.42, 8.36)	7.52 (5.77, 9.56)	6.23 (5.02, 7.78)	−1.930	0.054
	LYM($\times10^9$/L)	1.10–3.20	0.58 (0.25, 0.79)	0.25 (0.19, 0.62)	0.71 (0.50, 0.81)	−3.165	0.002
	Hb(g/L)	115–150	126 (112, 136)	118 (104.50, 127)	128 (117, 142)	−2.152	0.031
	PLT($\times10^9$/L)	125–350	162 (129, 195)	162.50 (107.50, 224)	161 (137, 183)	−0.405	0.685
	CRP(mg/L)	<8.0	148.72 (112.81, 182.10)	162.72 (143.28, 200)	126.24 (108.84, 166.45)	−1.741	0.082
Liver and Renal Function[M(Q1,Q3)]	ALT(U/L)	9–50	59 (31.50, 89)	77.65 (49.25, 99.75)	38.90 (22.00, 80.70)	−2.431	0.015
	AST(U/L)	15–40	67.60 (41.50, 132.20)	112 (68.90, 179.68)	43.60 (32.60, 80.50)	−3.598	<0.001
	TBIL(μmol/L)	2–25	15.30 (10.10, 21.20)	17.45 (10.83, 22.90)	14.80 (10.10, 18.80)	−0.984	0.325
	ALB(g/L)	40–55	35.80 (29.10, 40.30)	30.25 (27.45, 36.28)	36.50 (32.90, 42.70)	−2.701	0.007
	BUN(mmol/L)	3.20–7.14	5.48 (3.61, 8.80)	7.13 (3.27, 11.230)	5.07 (3.61, 7.65)	−0.820	0.412
	Cr(μmol/L)	40–135	71.80 (59.70, 99)	74.05 (58.55, 110.58)	71.80 (59.70, 96)	−0.424	0.671
	LDH(U/L)	114–240	289 (233, 402)	392.5 (320.75, 607.25)	236 (219, 303)	−3.570	<0.001
	CK-MB(U/L)	0–24	8 (6, 12.80)	8 (4.73, 13.30)	7.80 (6.20, 12.40)	−0.087	0.931
	CK(U/L)	25–200	100 (49, 239)	152.60 (65.50, 248)	71 (48, 235)	−1.119	0.263
Coagulation Profile [M(Q1,Q3)]	DD(μg/L)	<500	1380 (782, 3798)	2140.50 (1512.75, 5463.25)	942 (702, 1562)	−3.020	0.003
	TT(S)	10.30–16.60	13.70 (12.70, 14.80)	14.30 (12.55, 15.48)	13.70 (12.70, 14.30)	−1.178	0.239
	PT(S)	9.40–12.50	13.40 (12.40, 14.50)	13.95 (13.03, 14.78)	13.20 (12.30, 14.10)	−1.178	0.239
	APTT(S)	25.10–36.50	32.80 (30.10, 34.70)	32.20 (30.33, 34.90)	32.80 (30, 34.70)	−0.415	0.678
	FIB(g/L)	2.38–4.98	6.97 (6.42, 8.09)	7.325 (6.61, 8.67)	6.69 (6.24, 7.98)	−1.408	0.159

Abbreviations: TBIL: Total bilirubin; Cr: Creatinine; CK-MB: Creatine Kinase-MB Isoenzyme; CK: Creatine Kinase; TT: Thrombin time; PT: Prothrombin time; APTT: Activated partial thromboplastin time; FIB: Fibrinogen.

Table 3 Longitudinal Trends in Laboratory Parameters Between the Severe and Non-Severe Pneumonia Groups

	Normal Reference Range	All (N=51)	Severe (N=20)	Non-severe (N=31)	t/Z	p value
WBC($\times10^9$/L)	3.50–9.50					
Initial measurement#		7.61 (6.15, 9.70)	8.26 (6.87, 10.25)	7.56 (5.65, 9.09)	Z= −1.023	0.307
Second measurement#		5.66 (4.42, 8.62)	6.18 (5.02, 9.85)	5.06 (4.07, 7.63)	Z= −1.756	0.079
LYM($\times10^9$/L)	1.10–3.20					
Initial measurement#		0.575 (0.25, 0.79)	0.25 (0.19, 0.62)	0.71 (0.50, 0.81)	Z= −3.165	0.002
Second measurement#		0.59 (0.37, 0.91)	0.47 (0.22, 0.72)	0.75 (0.45, 1.09)	Z= −2.065	0.039
Hb(g/L)	115–150					
Initial measurement#		126 (112, 136)	118 (104.50, 127)	128 (117, 142)	Z= −2.152	0.031
Second measurement*		116.53±21.59	105.60±20.01	123.58±19.80	t=3.153	0.003
PLT($\times10^9$/L)	125–350					
Initial measurement#		162 (129, 195)	162.50 (107.50, 224)	161 (137, 183)	Z= −0.405	0.685
Second measurement#		167 (128, 219)	151.50 (115.50, 237.75)	172 (151, 215)	Z= −0.733	0.463
CRP(mg/L)	<8.0					
Initial measurement#		148.72 (112.81, 182.10)	162.72 (143.28, 200)	126.24 (108.84, 166.45)	Z= −1.741	0.082
Second measurement*		119.02±60.45	139.10±50.97	106.07±63.27	t=−1.958	0.056
NEU($\times10^9$/L)	1.80–6.30					
Initial measurement#		6.56 (5.42, 8.36)	7.52 (5.77, 9.56)	6.23 (5.02, 7.78)	Z= −1.930	0.054
Second measurement#		4.78 (2.86, 7.67)	5.59 (4.18, 11.04)	3.65 (2.78, 7.54)	Z= −2.209	0.072

Note:*Normality was confirmed by Shapiro–Wilk test ($p > 0.05$); # Non-normality was confirmed by Shapiro–Wilk test ($p < 0.05$).

Imaging Features

Patients in the severe pneumonia group exhibited a significantly higher proportion of bilateral lung involvement compared to those in the non-severe group ($p = 0.003$). Additionally, there was no statistically significant intergroup difference in the prevalence of consolidation, ground-glass opacities, and pleural effusion. Detailed imaging characteristics are summarized in Table 4.

Screening of Risk Factors and Multivariate Analysis Results

Variables that were statistically significant in the univariate analysis were further evaluated using VIF. The results revealed collinearity (VIF > 5) among Hb at the first measurement (VIF = 5.10), AST (VIF = 5.50), and LDH (VIF = 6.53). Based on physiological relevance and comprehensive considerations, Hb at the first measurement and AST were excluded. Finally, nine variables with low collinearity (all VIF < 5) were retained for subsequent analysis.

Lasso regression (with $\alpha = 1$) was applied to further screen the aforementioned nine variables. The optimal regularization parameter (λ_min) was selected through 5-fold cross-validation. Four variables most strongly associated with severe pneumonia were identified (Figures 1 and 2): CVD, LYM at the first measurement, Hb at the second measurement, and LDH.

A Firth-penalized logistic regression model was fitted using the four variables selected by Lasso (as shown in Table 5). The results indicated that a history of CVD was significantly associated with an increased risk of severe pneumonia (OR = 4.874, 95% CI: 1.270–22.763). A decreased Hb level at the second measurement was also significantly

Table 4 Imaging Findings of 51 Patients with Chlamydia Psittaci Pneumonia

	All (N=51)	Severe (N=20)	Non-severe (N=31)	χ^2	p value
Affected Region					
Unilateral Lung Involvement	33	8	25	8.794	0.003
Bilateral Lung Involvement	18	12	6		
Radiographic Abnormalities					
Consolidation	3	0	3	0.680	0.410
Ground-Glass Opacities	4	0	4	1.300	0.254
Pleural Effusion	24	11	13	0.833	0.361

https://doi.org/10.2147/IJGM.S545097

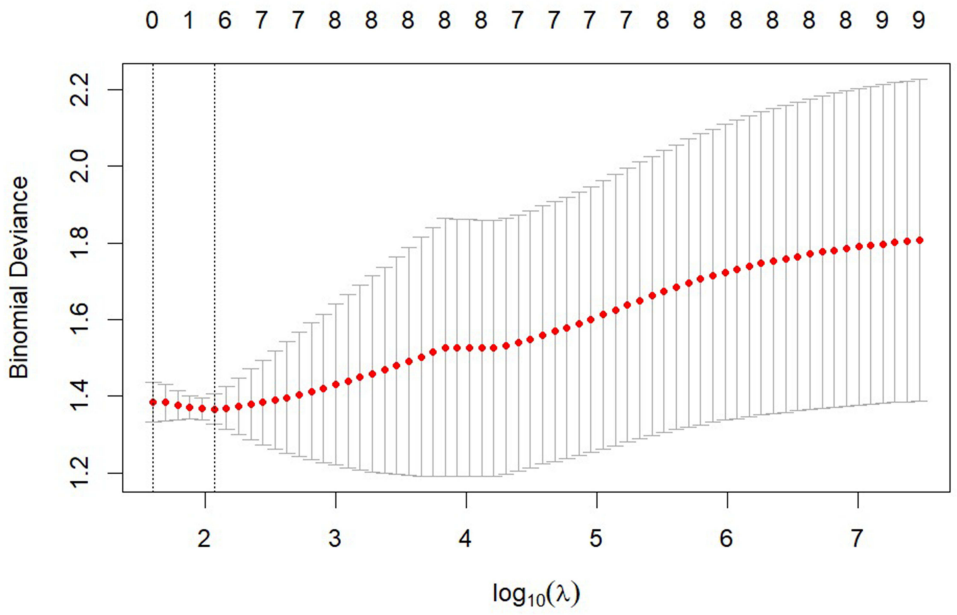

Figure 1 Five fold cross validation diagram.

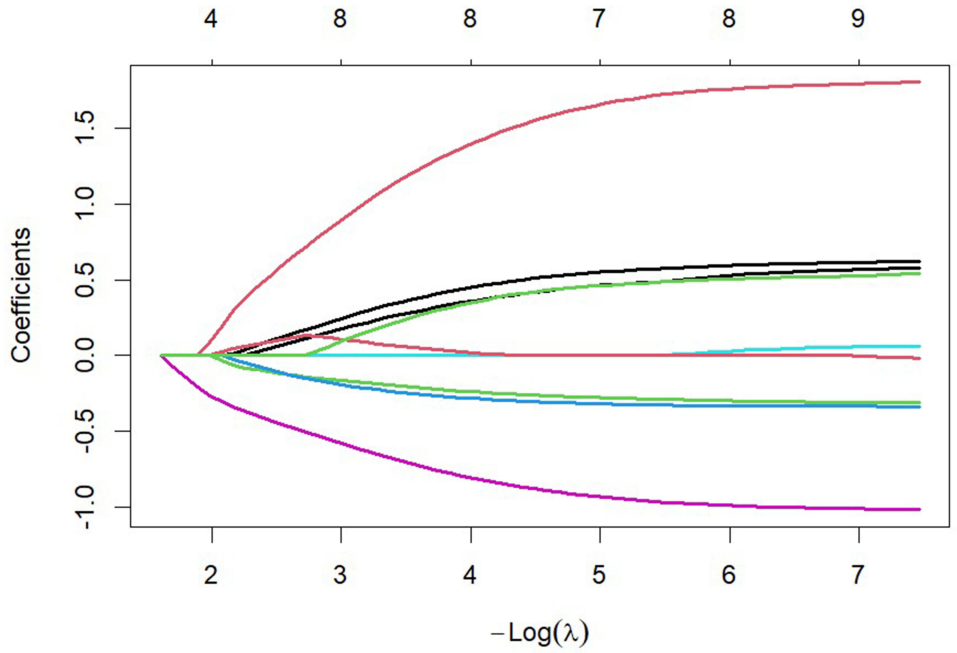

Figure 2 Convergence path diagram of LASSO regression coefficients.

associated with severe pneumonia risk (OR = 0.415, 95% CI: 0.169–0.844). In contrast, LYM at the first measurement (OR = 0.617) and LDH (OR = 1.570) did not reach statistical significance, with both 95% confidence intervals including 1.

Predictive Performance of Biomarkers

ROC curve analysis was conducted on laboratory markers showing statistically significant differences in univariate analysis. According to ROC curve analysis results, the following parameters showed good predictive value for severe

Table 5 Results of Firth-Penalized Logistic Regression for Risk Factors of Severe Pneumonia in Chlamydia Psittaci Pneumonia Patients

Variables	Coefficient	Standard Error	χ^2	p value	OR	95% CI
Intercept	−2.680	1.050	7.204	0.007	0.069	0.007–0.499
CVD	1.584	0.703	5.388	0.020	4.874	1.270–22.763
LYM at the first measurement	−0.483	0.363	1.716	0.190	0.617	0.276–1.276
Hb at the second measurement	−0.879	0.382	6.098	0.013	0.415	0.169–0.844
LDH	0.451	0.321	1.856	0.173	1.570	0.808–3.232

pneumonia progression: LYM at the first measurement, Hb at the second measurement, ALT, AST, ALB, LDH, and DD, all of which had an AUC > 0.7 (Figure 3 and Table 6). Notably, LYM at the first measurement and LDH exhibited both sensitivity and specificity exceeding 70%, qualifying them as robust predictors.

Predictive Performance of the Multivariate Model

ROC analysis confirmed the excellent predictive performance of the full multivariate model (AUC = 0.885; Table 7). Analysis of predictor combinations revealed distinct performance characteristics: incorporating LYM at the first measurement with CVD improved AUC, sensitivity, and specificity, whereas the addition of the second Hb measurement to CVD yielded high specificity (90.32%). The combination of CVD with LDH maintained the highest sensitivity (90%). The model with CVD alone demonstrated more limited predictive capacity.

Discussion

Among patients (aged 30–83 years, mean 60.61 years) in this study, patients in the severe pneumonia group showed significantly older age, aligning with previous reports of age-related disease progression.[11,12] This pattern may reflect the cumulative effects of immunosenescence (age-related decline in immune competence) and chronic low-grade inflammation in older adults.[13,14] Regarding exposure history, only 23.53% of patients reported definitive contact with birds. Additionally, two patients with no avian contact reported exposure to waste or recyclable materials. This observation aligns with sporadic reports,[15,16] and prior literature indicating that human infection can occur not only through direct contact with birds but also through indirect environmental exposure, such as handling feathers or tissues of infected birds.[4] No statistically significant differences were observed in gender or seasonal distribution in the present study. It is noteworthy, however, that two large-sample studies from Belgium and Southwest China both reported a significantly higher number of cases in males than in females.[17,18] Data from the Netherlands suggest that spring and summer are the

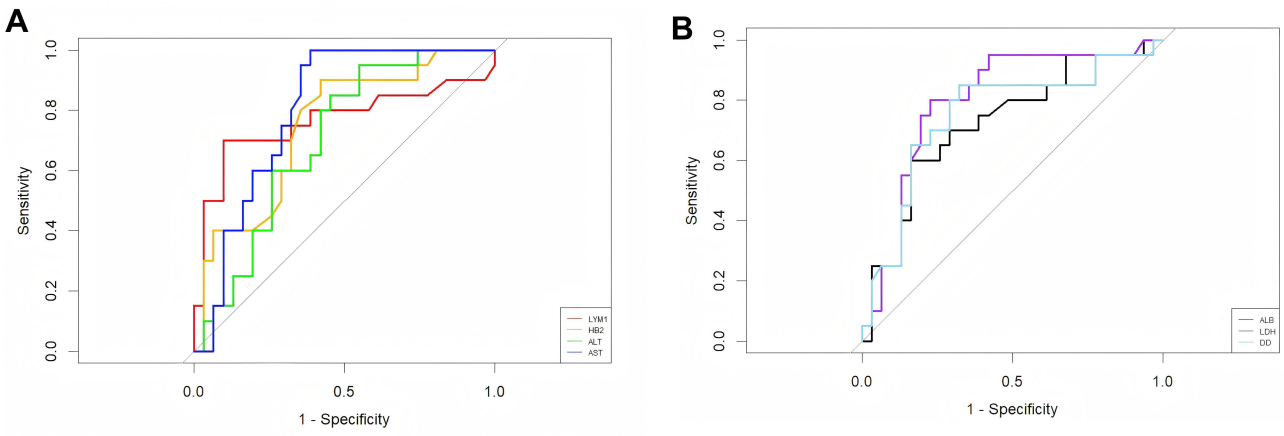

Figure 3 ROC curves of laboratory biomarkers for predicting severe pneumonia progression in psittacosis patients. (**A**) ROC curves for LYM at the first measurement, HB at the second measurement, ALT, and AST. (**B**) ROC curves for ALB, LDH, and DD.

https://doi.org/10.2147/IJGM.S545097

Table 6 ROC Curve Analysis of Laboratory Biomarkers for Predicting Severe Pneumonia Progression in Chlamydia Psittaci Pneumonia Cases

	AUC	p value	Cut-off	Sensitivity	Specificity	95% CI	Youden's Index
LYM at the first measurement	0.765	<0.001	0.425	70.0%	90.32%	0.607–0.922	0.603
Hb at the second measurement	0.747	<0.001	122.50	90%	58.06%	0.609–0.885	0.481
ALT	0.703	<0.001	34.65	95%	45.16%	0.560–0.846	0.402
AST	0.801	<0.001	50.50	100%	61.29%	0.679–0.923	0.613
ALB	0.726	<0.001	31.30	60%	83.87%	0.579–0.873	0.439
LDH	0.798	<0.001	308	80%	77.42%	0.668–0.929	0.574
DD	0.752	<0.001	1300	85%	67.74%	0.605–0.900	0.527

Table 7 Comparison of ROC Metrics for Different Variable Sets

Model	AUC	95% CI	Sensitivity	Specificity	Cut-off
CVD	0.655	0.518–0.792	60%	70.97%	0.421
CVD+LYM at the first measurement	0.777	0.635–0.919	75%	80.65%	0.418
CVD +Hb at the second measurement	0.818	0.689–0.947	70%	90.32%	0.517
CVD+LDH	0.778	0.645–0.911	90%	61.29%	0.244
Overall Model	0.885	0.787–0.984	75%	93.50%	0.448

peak seasons for infection,[19] whereas a multicenter study in China indicated a concentration of cases from September to April.[20] Given that these discrepancies may be attributable to differences in region, climate, and poultry trade patterns, future multicenter studies with larger sample sizes are warranted to further elucidate the epidemiological characteristics of psittacosis pneumonia.

Our study revealed heterogeneous clinical manifestations, with fever being the most prevalent symptom (observed in 98.04% of cases), followed by cough, fatigue, myalgia, headache, and diarrhea. *Chlamydia psittaci*, as an obligate intracellular pathogen, replicates within host cells through binary fission to form immune-evasive inclusion bodies.[21,22] The subsequent hematogenous dissemination induces pulmonary inflammation and multiple organ dysfunction involving the liver, spleen, and cardiac tissues. This pathogenic mechanism explains the multi-system clinical manifestations involving multiple organ systems.

Univariate analysis revealed that 60.0% of severe pneumonia cases had a pre-existing CVD, a proportion significantly higher than that in the non-severe group. Furthermore, Firth-penalized logistic regression analysis confirmed that a history of CVD was significantly associated with the risk of severe psittacosis pneumonia (OR = 4.874, $p = 0.020$). This finding is consistent with several existing studies. For example, Ni et al reported a statistically significant difference in the distribution of cardiovascular and cerebrovascular diseases between the severe and non-severe pneumonia groups.[23] However, in the study by Yang et al,[18] although a higher proportion of severe pneumonia cases had a history of CVD (7/53) compared to the non-severe group (3/63), the intergroup difference did not reach statistical significance. Similarly, studies by Yuan et al and Xu et al found no significant differences in the prevalence of hypertension or coronary heart disease between the two groups.[24,25] The inconsistency among these studies may stem from variations in sample size, population characteristics, or potential confounding factors, suggesting that the association between CVD and severe psittacosis pneumonia should be interpreted with caution.

Previous studies on psittacosis pneumonia patients have primarily analyzed laboratory parameters at isolated time points. In contrast, our study collected data from the first two consecutive laboratory tests (CBC and inflammatory markers) after hospital admission. Through dynamic monitoring, it was found that the severe pneumonia group exhibited marked lymphocytopenia (decreased absolute LYM) at initial presentation, with levels persistently lower than normal across both tests and demonstrating delayed recovery. Meanwhile, a gradual Hb decline was observed in severe cases. Notably, decreased Hb levels at the second measurement were significantly associated with an increased risk of severe

psittacosis pneumonia (OR = 0.415, $p = 0.013$). This finding aligns with the characteristics reported by Zhang et al in a case of fulminant psittacosis pneumonia with multiple organ failure, wherein a gradual decrease in Hb coexisted with thrombocytopenia and a marked elevation in DD.[26] This consistency suggests that a progressive decline in Hb may be an important accompanying feature in the progression to severe pneumonia.

This study observed that lymphocytopenia was present early in patients with severe disease. Although logistic regression analysis indicated that the 95% confidence intervals for both the initial LYM (OR = 0.62) and LDH (OR = 1.57) included 1, rendering these associations statistically non-significant, the direction of their effects was consistent with multiple previous studies. For instance, a study from Southwest China reported lymphocytopenia in 93% of critically ill patients with psittacosis.[27] Similarly, an analysis of 35 patients in Southern China found that counts of lymphocytes, $CD3^+$ T cells, and $CD4^+$ T cells were significantly lower in severe pneumonia patients than in non-severe cases.[25]

Univariate ROC curve analysis revealed that an LDH level ≥308 U/L demonstrated good discriminatory power for severe psittacosis pneumonia (AUC = 0.798, with both sensitivity and specificity exceeding 70%). LDH is a glycolytic enzyme widely present within cells, and elevated serum levels typically indicate cellular damage or necrosis. In psittacosis pneumonia, increased LDH may result from multi-organ involvement, including necrosis of alveolar epithelial cells, hepatocyte destruction, and myocardial cytolysis.[28,29] The LDH cutoff value established in this study (308 U/L) differs significantly from the threshold (473 IU/L) reported by Guo et al[30] for predicting liver injury. This discrepancy is primarily attributable to distinct research objectives: Guo et al focused on identifying liver injury, whereas our study aimed to predict the progression to severe pneumonia.

Further ROC analysis confirmed that the second Hb measurement and the first LYM each achieved an AUC of >0.7 when used alone. The subsequent inclusion of CVD history revealed distinct performance profiles among the variable combinations: the combination of CVD and the second Hb measurement yielded the highest AUC (0.818) and optimal specificity (90.32%), demonstrating its superiority in accurately identifying high-risk cases of severe pneumonia. In contrast, the combination of CVD and LDH exhibited the highest sensitivity (90%) but a relatively low specificity (61.29%), making it more suitable for initial screening of severe pneumonia risk. The final multivariable model, which integrated CVD history, the second Hb measurement, the first LYM, and LDH, demonstrated good discriminative capability, with an AUC of 0.885, a sensitivity of 75%, and a specificity of 93.50%, indicating promising potential for early clinical screening. Collectively, these findings provide evidence-based support for a structured and multi-dimensional approach to indicator selection to facilitate the early detection of severe psittacosis pneumonia.

Furthermore, in the present study, the severe pneumonia group exhibited significantly higher rates of bilateral lung involvement, suggesting that this radiographic pattern may serve as a prognostic indicator for disease progression. Although previous studies have described characteristic findings, including consolidation with air bronchograms,[31] mixed ground-glass and consolidative opacities,[23] and reticular patterns,[32] psittacosis pneumonia generally lacks pathognomonic imaging features compared to other pneumonia. Nevertheless, even in the absence of specificity, rapid bilateral progression still warrants clinical vigilance, as it's a potential sentinel marker of deterioration that needs to be comprehensively assessed in conjunction with laboratory parameters.

As a single-center retrospective study, this research has inherent limitations: the relatively small sample size (n = 51) may have limited the statistical power, and parameters such as BNP were excluded due to incomplete data. Despite these limitations, this study employed dynamic monitoring of laboratory indicators and developed multivariable predictive models, thus helping to elucidate the potential roles of CVD history, progressive decrease in Hb, persistent lymphocytopenia, and elevated LDH in the severity progression of psittacosis. The final model demonstrated good performance, providing an objective, multi-dimensional framework for the early identification of high-risk cases. Future larger-scale, multicenter prospective studies are warranted to validate the efficacy of this model and to explore additional biomarkers. Such efforts could help optimize early warning strategies for severe psittacosis pneumonia and improve patient prognosis.

Abbreviations

EWRS, Early Warning and Response System of the European Union; CAP, community-acquired pneumonia; mNGS, metagenomic next-generation sequencing; PCR, polymerase chain reaction; BALF, bronchoalveolar lavage fluid; EMR, electronic medical records; CBC, complete blood count; WBC, white blood cell count; LYM, lymphocyte count; Hb,

hemoglobin; PLT, platelet count; CRP, C-reactive protein; NEU, neutrophil count; CT, computed tomography; BUN, blood urea nitrogen; BNP, B-type natriuretic peptide; VIF, variance inflation factor; LASSO, least absolute shrinkage and selection operator; ROC, Receiver operating characteristic; AUC, area under the curve; CVD, cardiovascular diseases; ALB, albumin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDH, lactate dehydrogenase; DD, D-dimer; TBIL, Total bilirubin; Cr, Creatinine; CK-MB, Creatine Kinase-MB Isoenzyme; CK, Creatine Kinase; TT, Thrombin time; PT, Prothrombin time; APTT, Activated partial thromboplastin time; FIB, Fibrinogen.

Data Sharing Statement

The datasets used or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Statement and Informed Consent

The study protocol was approved by the Ethics Committee of Affiliated Jinhua Hospital, Zhejiang University School of Medicine (2025-ethical review-137). As this is a retrospective study based on the collection of previously recorded clinical data, the Ethics Committee of Affiliated Jinhua Hospital, Zhejiang University School of Medicine granted a waiver of informed consent. Additionally, we declare that this study was conducted in accordance with the Declaration of Helsinki, and the patient related data is strictly confidential.

Acknowledgments

The authors thank all patients involved in the study.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This research was funded by the Science and Technology Bureau of Jinhua, grant number 2022-4-126.

Disclosure

The authors have declared that no competing interests exist in this work.

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