ORIGINAL RESEARCH

Analysis of Clinical Characteristics and Severe Factors of 47 Cases of Psittacosis

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Purpose: Analyze the epidemiology, clinical manifestations, and imaging characteristics of 47 patients with psittacosis, combined with laboratory indicators, to explore influencing factors and early warning indicators of severe psittacosis.

Patients and Methods: The analysis was conducted on case data of patients with psittacosis admitted to The Affiliated Changsha Hospital of Xiangya School of Medicine, Central South University, from January 2021 to September 2024, comparing differences between non-severe and severe patients, analyzing the correlation and impact degree between laboratory indicators and severity of the illness, finding independent influencing factors for the progression of psittacosis patients to severe.

Results: The mean age of 47 patients was 61.53. 61.70% of patients were male. Most patients were retired and self-employed (23.40%). A clear history of exposure to poultry was observed in 36.17% of patients. These were mainly associated with hypertension (31.91%), cerebral infarction (10.64%), and Acquired Immune Deficiency Syndrome (10.64%). The median time from disease onset to hospitalization was 5 days. The median length of the hospital stay was 10 days. 85.11% of patients had fever. Chest CT features were mainly pulmonary lobe infectious lesions (93.62%). Compared with non-severe patients, severe patients had higher levels of aspartate aminotransferase, lactate dehydrogenase, D-dimer, C-reactive protein, and procalcitonin ($P < 0.05$). LDH, D-dimer, CRP, and PCT levels positively correlated with severe psittacosis ($r > 0$, $P < 0.05$). D-dimer level was an independent risk factor for the progression of psittacosis to severe disease ($OR > 1$, $P < 0.05$), with an AUC of 0.761. The optimal threshold was 2.50μg/mL, with 66.70% sensitivity and 78.80% specificity.

Conclusion: Forty-seven patients with psittacosis were mainly elderly males, with fever as the typical symptom. Chest CT revealed infectious lesions in the lung lobes. D-dimer level could be an independent factor for the early warning of severe psittacosis.

Keywords: psittacosis, d-dimer, severe illness, influencing factors, early warning

Introduction

Psittacosis is a global and underestimated animal borne disease, with increasing cases reported in many countries. There have been multiple outbreaks of psittacosis in China, with even fatalities. According to reports from Austria, Denmark, Germany, Sweden, and the Netherlands, there has been an abnormal and unexpected increase in cases of psittacosis from early 2023 to early 2024. Psittacosis is a zoonotic disease, also known as avian chlamydial, ornithosis, or parrot disease. It is caused by *Chlamydia psittaci* and is mainly transmitted from birds to humans.[1] *Chlamydia psittaci* is a gram-negative bacterium that can cause atypical pneumonia when infecting the lungs. It can be transmitted to humans through direct contact with animals, avian secretions and excreta, and inhalation of feather dust.[2] Mild patients with *Chlamydia psittaci* pneumonia mainly present with flu like symptoms such as fever, sore throat, and cough. Severe patients may develop severe pneumonia, myocarditis, endocarditis, renal insufficiency, encephalitis, and even death. Due to the lack of specificity in its clinical manifestations and the difficulty in detecting *Chlamydia psittaci* through routine testing, clinical diagnosis is difficult. The preferred treatment for *Chlamydia psittaci* pneumonia is *doxycycline* or *minocycline*, followed by *macrocyclic esters*. *Quinolones* also have good clinical efficacy.[3] The latest research shows that *Chlamydia psittaci*

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has multiple transmission routes among humans, not only between infected individuals and contacts but also between mothers and children. Asymptomatic carriers can also transmit the pathogens. It has been reported that the mortality rates of psittacosis in the fetus and mother are 82.6% and 8.7%, respectively.[4] In recent years, with the continuous update of diagnostic technology, metagenomic next-generation sequencing (mNGS) can detect *Chlamydia psittaci* quantitatively, rapidly, and accurately.[5] This study summarizes the clinical manifestations and imaging results of 47 patients with psittacosis diagnosed by mNGS at The Affiliated Changsha Hospital of Xiangya School of Medicine, Central South University in the past 4 years, by comparing the differences in laboratory indicators between severe and non-severe patients and exploring the risk factors and warning indicators of severe patients to provide experience for early identification of severe patients with psittacosis.

Material and Methods
Case Source
Using retrospective analysis, we collected case data from patients with psittacosis admitted to The Affiliated Changsha Hospital of Xiangya School of Medicine, Central South University from January 2021 to September 2024. All diagnoses of patients were based on the "Consensus of Chinese Experts on Psittacosis Diagnosis and Treatment (2024)".[6] They had epidemiological history, clinical and imaging manifestations of psittacosis. All patients tested positive for Chlamydia psittaci nucleic acid in the bronchoalveolar lavage fluid or blood samples using mNGS. The BGI sequencing platform is used for mNGS. mNGS workflow includes two components: experimental manipulations (wet lab) and bioinformatic analysis (dry lab). The wet lab manipulations include sample preprocessing, nucleic acid extraction, library preparation, and sequencing. The dry lab bioinformatic analysis includes quality control of data, removal of human sequences and sequence alignment of sequences from microbial species. Patients with severe psittacosis are defined as the occurrence of respiratory failure, acute respiratory distress syndrome, and multiorgan system failures. Respiratory failure is defined as an oxygenation index <400 mmHg (1 mmHg = 0.133 kPa).[6] This study excluded patients with incomplete case data.

Data Collection
The hospital information management system, laboratory information management system, and electronic medical record system collected the following observation indicators: age, sex, occupation, clinical manifestations, medical history, exposure history, onset-to-hospitalization time, length of hospital stay, white blood cell count (WBC), neutrophils (N), lymphocytes (L), erythrocyte sedimentation rate (ESR), fibrinogen (FIB), serum sodium, alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatine kinase (CK), lactate dehydrogenase (LDH), D-dimer, C-reactive protein (CRP), procalcitonin (PCT), oxygen partial pressure, carbon dioxide partial pressure, and chest computed tomography (CT) results on the first day of admission.

Statistical Analysis
Statistical analyses were performed using SPSS 25.0. Count data are presented as n (%). The comparison of count data between the groups was conducted using the chi-squared test. Metric data are presented as mean ± standard deviation (*SD*). The comparison of metric data between groups was conducted using an independent sample *t*-test. Measurement data with skewed distribution are displayed as median and interquartile range [*M (P25, P75)*]. The Mann–Whitney *U*-test was used for intergroup comparisons. Adopting bivariate correlation analysis to investigate the correlation between laboratory indicators and the severity of the illness, $r > 0$ indicated a positive correlation, $r < 0$ indicated a negative correlation, $r = 0$ indicated complete independence, $r = 1$ indicated complete correlation. The closer $| r |$ is to 1, the stronger the correlation. Using the condition (non-severe/severe) as the dependent variable and laboratory indicators as independent variables, a univariate binary logistic regression analysis was conducted to obtain the odds ratio (*OR*) and 95% confidence interval (*CI*), and to screen for independent prognostic factors. Receiver operating characteristic (ROC) curves were used to analyze the predictive power of laboratory indicators for severe psittacosis and calculate the area under the curve (AUC). P-value lower at 0.05 ($P < 0.05$) was considered for significant differences.

Results

Epidemiological Characteristics

The average age of the 47 patients with psittacosis was 61.53 years old, and the majority were male (61.70%). Retired personnel and freelancers account for 23.40%. A clear history of contact with poultry was observed in 36.17% of patients. The main comorbid diseases were hypertension (31.91%), cerebral infarction (10.64%), and AIDS (10.64%). The median time from disease onset to hospitalization was 5 days. The median length of the hospital stay was 10 days (Table 1).

Clinical Manifestations

Most patients had fever (85.11%), followed by cough (46.81%), expectoration (19.15%), and headaches (12.77%) (Table 2).

Chest CT Characteristics

Most patients had infectious lung lobe lesions (93.62%), followed by pleural effusion (42.55%), and pulmonary consolidation (29.79%) (Table 3).

Laboratory Tests

Compared to non-severe patients, severe patients had higher levels of AST, LDH, D-dimer, CRP, and PCT ($P < 0.05$), while there were no statistically significant differences in the levels of WBC, N, L, ESR, FIB, serum sodium, ALT, CK, oxygen pressure, or carbon dioxide pressure ($P > 0.05$). Moreover, the levels of serum sodium, oxygen pressure, and

Table 1 Patient Population and Epidemiological Characteristics

Variables	N = 47
Sex [N (%)]	
Male	29 (61.70)
Female	18 (38.30)
Age (years)	61.53 ± 11.71
Duration from onset to hospitalization (days)	5.00 (4.00, 9.00)
Length of hospital stay (days)	10.00 (9.00, 12.00)
Occupation [N (%)]	
Retired personnel	11 (23.40)
Freelancer	11 (23.40)
Farmer	7 (14.89)
Worker	7 (14.89)
Individual business	5 (10.64)
Unemployed	5 (10.64)
Company employee	1 (2.13)
Exposure history [N (%)]	
Contact with poultry	17 (36.17)
Not clear	30 (63.83)
Underlying disease [N (%)]	
Hypertension	15 (31.91)
Coronary heart disease	4 (8.51)
Diabetes	4 (8.51)
Cerebral infarction	5 (10.64)
Chronic obstructive pulmonary disease	4 (8.51)
Hepatic insufficiency	4 (8.51)
Pulmonary tuberculosis	3 (6.38)
Bronchitis	2 (4.26)
AIDS	5 (10.64)

Table 2 Clinical Manifestations of Patients [N (%)]

Variables	N = 47
Fever	40 (85.11)
Cough	22 (46.81)
Expectoration	9 (19.15)
Shortness of breath	3 (6.38)
Dizziness	4 (8.51)
Headache	6 (12.77)
Fatigue	2 (4.26)
Poor appetite	1 (2.13)
Oliguria	1 (2.13)
Myalgia	1 (2.13)
Arthralgia	1 (2.13)
Chest tightness	1 (2.13)
Sickness	1 (2.13)

Table 3 Chest CT Characteristics of Patients [N (%)]

Variables	N = 47
Infectious lesions of lung lobes	44 (93.62)
Pleural effusion	20 (42.55)
Pulmonary consolidation	14 (29.79)
Pulmonary emphysema	9 (19.15)
Pulmonary nodule	6 (12.77)
Ground-glass opacity	4 (8.51)
Pleurisy	2 (4.26)
Infectious lesions of pulmonary interstitial	1 (2.13)

carbon dioxide pressure were lower than the normal range, while ESR, FIB, ALT, AST, LDH, D-dimer, CRP, and PCT levels were higher than the normal range. Additionally, the average absolute value of L in severe patients was lower than the normal range (Table 4).

Correlation Analysis Between Laboratory Indicators and Severity of the Illness

LDH, D-dimer, CRP, and PCT levels were positively correlated with severe psittacosis ($r > 0$, $P < 0.05$). However, the correlation between the levels of CRP, PCT, LDH and the severity of the disease is poor ($0.2 \leq |r| < 0.4$, $P < 0.05$) (Table 5).

Independent Influencing Factors of Severe Psittacosis

D-dimer level was an independent risk factor for the progression of severe psittacosis ($OR > 1$, $P < 0.05$) (Table 6).

Predictive Value of D-Dimer for Severe Psittacosis

The ROC curve was used to evaluate the warning efficacy of D-dimer for severe psittacosis, with an area under the curve of 0.761 ($P < 0.01$). When the D-dimer cut-off value was 2.50, the sensitivity and specificity for predicting severe psittacosis were 66.70% and 78.80%, respectively (Table 7 and Figure 1).

Discussion

Chlamydia psittaci is an obligate intracellular gram-negative bacterium that primarily infects birds and causes zoonotic infections. Humans are usually infected by inhaling aerosols from the excrement of infected birds.[7] The clinical

Table 4 Comparison of Laboratory Tests Between Non Severe and Severe Patients

Variables	Non Severe Patients (N = 35)	Severe Patients (N = 12)	Statistical Value	P Value
WBC (×10⁹/L)	7.73 ± 2.80	7.79 ± 2.32	$t = -0.06$	0.949
N (×10⁹/L)	5.92 ± 2.50	6.09 ± 2.27	$t = -0.20$	0.840
L (×10⁹/L)	0.94 ± 0.49	0.73 ± 0.42	$t = 1.36$	0.182
ESR (mm/h)	79.81 ± 26.54	89.50 ± 22.83	$t = -1.11$	0.270
FIB (g/L)	6.64 ± 0.99	6.45 ± 2.21	$t = 0.29$	0.776
Serum sodium (mmol/L)	134.33 ± 5.10	134.04 ± 5.06	$t = 0.17$	0.866
ALT (U/L)	50.30 ± 36.47	74.58 ± 55.06	$t = -1.42$	0.177
AST (U/L)	43.65 (22.08, 86.10)	113.00 (39.95, 297.73)	$Z = -2.67$	0.008
CK (U/L)	147.70 (63.28, 297.13)	171.70 (107.00, 724.33)	$Z = -1.13$	0.259
LDH (U/L)	251.00 (214.45, 363.00)	337.50 (270.25, 562.00)	$Z = -2.27$	0.023
D-dimer (mg/L)	1.58 (0.81, 2.48)	2.71 (1.57, 4.10)	$Z = -2.66$	0.008
CRP (mg/L)	136.31 ± 74.09	194.05 ± 97.12	$t = -2.15$	0.037
PCT (mg/L)	0.26 (0.08, 0.83)	0.85 (0.17, 5.19)	$Z = -2.03$	0.042
Oxygen pressure (mmHg)	86.60 ± 17.94	83.74 ± 17.82	$t = 0.47$	0.638
Carbon dioxide pressure (mmHg)	31.21 ± 6.89	31.78 ± 5.12	$t = -0.26$	0.798

Abbreviations: WBC, white blood cell; N, neutrophil; L, lymphocyte; ESR, erythrocyte sedimentation rate; FIB, fibrinogen; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CK, creatine kinase; LDH, lactic dehydrogenase; CRP, C-reactive protein; PCT, procalcitonin.

Table 5 Correlation Analysis Between Laboratory Indicators and Severity of the Illness

Variables	r Value	P Value
AST (U/L)	0.25	0.096
LDH (U/L)	0.34	0.021
D-dimer (mg/L)	0.40	0.006
CRP (mg/L)	0.31	0.037
PCT (mg/L)	0.31	0.041

Abbreviations: AST, aspartate aminotransferase; LDH, lactic dehydrogenase; CRP, C-reactive protein; PCT, procalcitonin.

Table 6 Single Factor Binary Logistic Regression Analysis of Laboratory Indicators and Early Warning of Severe Psittacosis

Variables	B	S.E.	Wald	df	P	OR	95% CI	
							Lower Limit	Upper Limit
LDH (U/L)	0.000	0.003	0.004	1	0.951	1.000	0.995	1.006
D-dimer (mg/L)	1.168	0.549	4.518	1	0.034	3.214	1.095	9.433
CRP (mg/L)	−0.011	0.008	1.808	1	0.179	0.989	0.973	1.005
PCT (mg/L)	0.884	0.474	3.471	1	0.062	2.420	0.955	6.134

Abbreviations: LDH, lactic dehydrogenase; CRP, C-reactive protein; PCT, procalcitonin.

manifestations of psittacosis are similar to influenza, including headache, fever, muscle pain, cough, and shortness of breath.[8] Our study confirmed this feature, with fever being the most prominent clinical symptom for patients. The patient's body temperature is usually above 39 °C, with the highest reaching 41 °C.

Table 7 ROC Curve of D-Dimer for Predicting the Severity of Psittacosis

Index	Cutoff (mg/L)	AUC	P Value	Sensitivity (%)	Specificity (%)	95% CI	
						Lower Limit	Upper Limit
D-dimer	2.50	0.761	0.008	66.70	78.80	0.595	0.928

With early identification and appropriate antibiotic treatment, psittacosis rarely leads to death. However, because of the frequent use of cell culture and serological testing before 2019, which requires high standards from laboratories and operators, and the lack of diagnostic timeliness in serological testing, it was difficult to determine the type of chlamydia, making diagnosis extremely challenging. This led to the worsening of the patient's illness, developing into explosive severe pneumonia and multiple organ failure.[9] With the popularization of mNGS in clinical practice, there have been increasing reports of cases of psittacosis. There have been a series of case reports on psittacosis pneumonia; however, the sample size was relatively small. In this study, we collected case data from 47 patients with psittacosis over the past 4 years. By expanding the sample size, we observed the clinical characteristics and analyzed the risk factors for severe illness, thus providing a basis for the early identification of severe patients.

The average age of patients in our study was 61.53 years, with male patients accounting for 61.70%, which was similar to the studies of Tianyun Shi,[10] Anbing Zhang,[11] and Yubo Huang.[12] Because the majority of patients were elderly, most of them
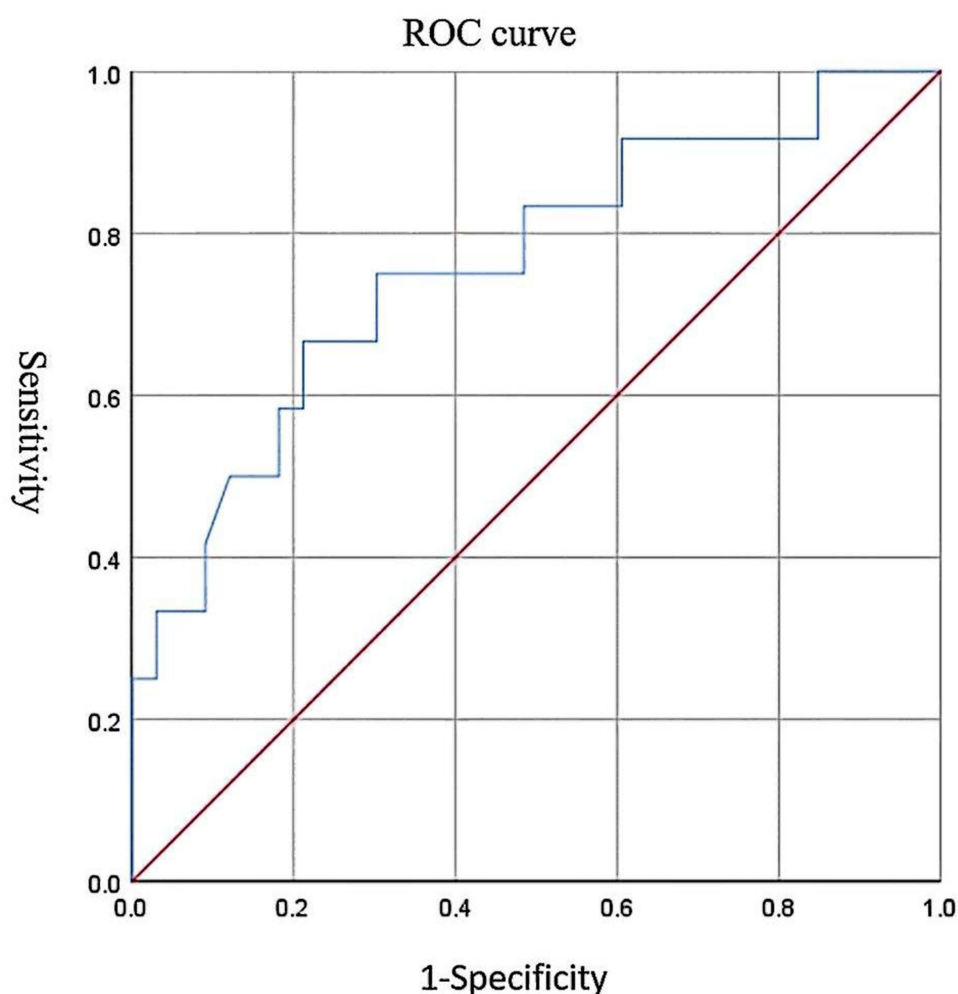
Figure 1 ROC curve analysis of diagnostic efficacy of D-dimer.

had comorbidities of hypertension and cerebral infarction. Mycoplasma psittaci infection is not uncommon in AIDS patients, which is one of the newly reported pathogens of AIDS patients complicated with lung infection in recent years.[13] Retired individuals and freelancers were more susceptible to psittacosis, as they may had more opportunities to come into contact with pet birds in pet stores and chickens, ducks, and pigeons in agricultural markets.[14] The history of exposure to poultry is an important basis for diagnosing psittacosis,[6] but only one-third of patients clearly indicate a history of exposure. According to research,[15] Chlamydia psittaci can survive at least 72 h at temperatures below 56°C and for several months in dry bird feces. It is possible that most patients are exposed to indirect environments such as accidental contact with contaminated bird secretions or excrement, which can lead to infection. The median time from disease onset to hospitalization was 5 days. The median length of the hospital stay was 10 days. There were similar to the statistics of Weizhong Jin.[16] Our study found that chest CT scans of patients often present with infectious lesions in the lung lobes, pleural effusion, and consolidation, which was similar to reports by Ying Gao,[17] Juan Jiang,[18] and Xiang Chen.[19] The occurrence of pleural effusion in psittacosis pneumonia may be more common than lung infections caused by other pathogens,[19] suggesting that healthcare workers need to consider the possibility of Chlamydia psittaci infection when discovering patients with such characteristics.

The laboratory test results showed that unlike pneumonia caused by other bacteria, WBC and N counts were within the normal range, which was consistent with the research of Yannick Vande Weygaerde[20] and helps clinical workers to exclude other traditional pneumonia bacterial infections. Although there was no significant difference in the average absolute value of L in severe patients compared with non-severe patients, it was lower than the normal range, which may be due to the weakened immune system in severe patients.[21] Some patients had type I respiratory failure, with oxygen and carbon dioxide partial pressures below the normal range. The levels of ESR, CRP, PCT, and FIB were also associated with infection. ESR is used to reflect the aggregation of FIB and immunoglobulin in the body and can increase the inflammatory response after 2 days.[22] CRP is synthesized by liver cells and is an acute phase response protein that rapidly rises after tissue damage and under the action of inflammatory factors. PCT is a protein produced and secreted by thyroid C cells, and consists of calcitonin, an N-terminal disabled fragment, and calcitonin. It significantly increases after acute or chronic pneumonia. FIB is present in human plasma and is commonly used to test coagulation function. When the body experiences inflammatory reactions, circulatory disorders, and high viscosity, it affects coagulation function and causes changes in coagulation index levels.[23] The levels of ALT, AST, and LDH rise indicate liver and myocardial damage. ALT is mainly present in the cytoplasm of liver cells, whereas AST is mainly present in myocardial cells, followed by the liver cell mitochondria. When the liver is damaged, the permeability of the liver cell membrane increases, large amounts of ALT and AST are released into the liver cells.[24] LDH mainly exists in myocardial cells. Once myocardial cells are damaged, AST and LDH enter the bloodstream.[25] The levels of CRP, PCT, AST, and LDH in severe patients increase significantly, which is similar to the results of the study by Shi.[10] Our experiment found that the levels of CRP, PCT, and LDH were positively correlated with the severity of the disease. However, these correlations are relatively low. This may be related to the fact that CRP and PCT mainly reflect bacterial infections, and not all patients have myocardial damage. The level of serum sodium was below the normal range, which was consistent with the statistical results of Cheng Ying Kong[26] and Xiang Chen.[19] It is worth noting that this study found that the level of D-dimer in psittacosis patients was higher than the normal range. D-dimer increase was more pronounced in severe patients than in non-severe patients and positively correlated with the severity of the condition, which has rarely been reported before. D-dimer is released after the degradation of cross-linked fibrin polymer, reflecting the level of fibrin polymer in the plasma, which is commonly used to assess coagulation function. When the levels of inflammatory mediators rise in patients, the coagulation system is activated, forming microthrombi, resulting in the level of D-dimer increased.[27] We through binary logistic regression analysis and ROC curve found that D-dimer was an independent risk factor for the progression of severe psittacosis in patients. When D-dimer ≥ 2.50 mg/L, it has high sensitivity and specificity in predicting the severity of psittacosis, indicating that the hypercoagulable state of blood in patients with psittacosis deserves high attention from physicians.

This study has some limitations. Firstly, the study cases were sourced from a single center, with the sample source limited. Secondly, the inter group comparison in this study did not take into account the confounding factors caused by comorbidities. It may have some impact on the logistic regression and ROC curve results. Last, the severity of pneumonia, such as the pneumonia severity index and CURB-65 score, has not yet been evaluated in detail. In the future, we will improve the analysis to provide a more theoretical basis for early identification and intervention in patients with severe psittacosis.

Conclusion

Our study analyzed the population characteristics, epidemiological history, clinical manifestations, laboratory test results, and imaging results of patients with psittacosis. It is believed that psittacosis is common in elderly males, with the majority of retirees and freelancers. History of contact with poultry is an important diagnostic criterion. The main clinical symptoms are fever, cough, sputum production, and headaches. Chest CT revealed infectious lesions in the lung lobes, pleural effusion, and pulmonary consolidation. Moreover, LDH, D-dimer, CRP, and PCT levels positively correlated with disease severity. However, the correlation between the levels of CRP, PCT, LDH and the severity of the disease is relatively low. In addition, D-dimer level could be an independent risk factor for the progression of psittacosis to severe illness.

Data Sharing Statement

The datasets for this study are available from the corresponding authors on reasonable request.

Ethics Approval and Consent to Participate

This study was conducted in accordance with all relevant tenets of the Declaration of Helsinki and approved by the Medical Ethics Committee of the First Hospital of Changsha (China) (Approval Number: 2024 Ethical Rapid Review [Clinical Article] No. 24) without the need. Written informed consent was not required. Data were extracted from routine clinical records and transferred to an anonymized, password-protected database that was securely maintained and did not contain personally identifiable information.

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.

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Disclosure

The authors report no conflicts of interest in this work.

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