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Epidemiology of Pertussis and the Screening Value of WBC and Lymphocyte Percentage

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Objective: Pertussis is a highly contagious respiratory disease, and early diagnosis and timely treatment are crucial for reducing complications and transmission. In this study, we analyzed the prevalence of pertussis and assessed the value of the WBC and lymphocyte percentage in its screening.

Methods: A retrospective analysis was conducted on global pertussis data from the past decade. Patients who recently underwent pertussis nucleic acid detection and complete blood count (CBC) in our hospital were selected. Based on the results, 538 patients were classified into the pertussis group, and 595 into the control group. White blood count (WBC) and lymphocyte percentages were compared, diagnostic efficacy was calculated, and evaluate their application value in the diagnosis of pertussis.

Results: In the past decade, the global incidence of pertussis first decreased, then increased. In China and Zhejiang province, it fluctuated but showed an upward trend recently. In Zhejiang Province, pertussis was more prevalent in summer and winter and rose last year. Between 2018 and 2020, most pertussis cases in China were infants under 1 year old. Last year, only 1.12% of patients in our hospital were infants, with more patients over 5 years old. WBC, lymphocyte percentage, and platelet count (PLT) was higher in the pertussis group ($P < 0.05$). Logistic regression showed that WBC, lymphocyte percentage, and PLT were correlated with pertussis infection. Sequential analysis showed that the WBC, lymphocyte percentage, and Youden's index for both combined were 0.124, 0.082, and 0.044, respectively.

Conclusion: The global incidence of pertussis is rising, with significant increases among adolescents and adults. Improved prevention and control strategies are needed. WBC and lymphocyte percentage serve as auxiliary diagnostic indicators, but their efficacy is limited.

Keywords: pertussis, epidemiology, WBC, lymphocyte percentage, diagnostic competence

Introduction

Pertussis is an acute respiratory infectious disease caused by the Bordetella pertussis bacteria. Before the popularization of vaccines containing pertussis components, populations were highly susceptible to this disease, particularly infants and young children.[1] The immunization coverage rate has increased dramatically since the 1980s, so the number of patients with pertussis worldwide has dropped by more than 90%. However, this disease has not been effectively controlled around the globe.[2] Besides, a "pertussis relapse" has occurred in many countries that have higher immunization coverage rates due to immunity attenuation and the mutation of the Bordetella pertussis bacteria after vaccination.[3,4] Pertussis is a highly contagious disease that is mainly transmitted through airborne droplets. Early symptoms such as mild cough, runny nose, and low-grade fever are similar to those of the common cold, which may lead to missed diagnoses or misdiagnoses.[5] Macrolide antibiotics are the preferred drugs for pertussis treatment, and the early administration of these drugs after the onset of pertussis generally achieves favorable therapeutic effects. However, the therapeutic effect is significantly lower if the antibiotics are administrated 1–2 weeks after onset.[3] Furthermore, improper treatment may

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result in serious complications, especially in infants and young children, including pneumonia, brain damage, apnea, and even death.[6] An early pertussis diagnosis ensures that patients promptly receive appropriate antibiotic treatment, which mitigates symptoms, shortens the course of the disease, and reduces the risk of complications. Thus, it is of great clinical significance to identify the risk factors and make timely diagnoses for patients with pertussis.

Recent studies have shown that white blood cell count (WBC), lymphocyte ratio, and platelet estimation have important clinical implications in the diagnosis of pertussis. Leukocytosis may be a common sign of infection, especially bacterial infection, which allows physicians to focus on other signs and symptoms of infection when evaluating patients.[7] In the case of pertussis, the proportion of lymphocytes may be elevated, which is similar to the viral disease in children.[8] In addition, indirect inflammatory markers such as platelet-lymphocyte ratio (PLR) and neutrophil-lymphocyte ratio (NLR) may also play a role in the evaluation of pertussis.[8] Therefore, considering these blood indices comprehensively could help clinicians to more accurately diagnose and manage in patients with pertussis.[9]

Currently, there are three methods for making a laboratory diagnosis for patients with pertussis, including Bordetella pertussis culture, Bordetella pertussis nucleic acid detection, and serum pertussis toxin antibody determination.[10] A bacterial culture of pertussis is highly specific, allowing for the identification of the pathogen, the evaluation of antibiotic sensitivity, and the support of epidemiological research as well as the confirmation of other test results. However, this method utilizes cumbersome procedures and is time-consuming, so it cannot meet the requirements of the rapid clinical diagnosis and treatment of pertussis.[11] The polymerase chain reaction (PCR) is characterized by simple procedures, rapid detection, and higher sensitivity, specificity, and negative predictive values. Nevertheless, PCR has special laboratory requirements and is not readily applicable in primary hospitals.[12] Serological antibody detection results may be affected by numerous factors such as the disease course and the individual vaccination time. As a result, the clinical application value of this method is not as high as that of Bordetella pertussis culture and nucleic acid detection.[13] Besides, the laboratory detection of pertussis is also affected by certain factors such as the specimen collection process, sampling time, vaccine immunization history, and antibiotic administration. Moreover, PCR and Bordetella pertussis culture are not sensitive in the advanced stages of this disease and there are some defects in the serological detection methodology.

Although the number of pertussis cases is increasing, the overall number of pertussis patients in our country is relatively low. Additionally, most pertussis patients exhibit clinical symptoms similar to those of respiratory infections, resulting in most initial diagnoses being made in primary hospitals. Meanwhile, since PCR is the primary diagnostic method for pertussis in our country, and most primary hospitals have not yet implemented PCR testing. Therefore, in primary hospitals, it is still necessary to use commonly used emergency inflammatory indicators in combination with clinical experience to assist clinicians in diagnosing pertussis. Although the prevalence of pertussis has increased recently, clinicians' experience in the diagnosis and treatment of this disease is still insufficient due to the relatively small number of patients in each hospital. In this study, the data related to pertussis nucleic acid detection and complete blood count (CBC) from June 1, 2023, to May 31, 2024, were retrospectively analyzed to assess the prevalence of pertussis and clarify the clinical significance of relevant indicators in the screening of this disease.

Methods and Subjects

Subjects

Epidemiological data concerning pertussis were collected from the World Health Organization (WHO), the National Disease Control and Prevention Administration, and the Health Commission of Zhejiang Province.[14–16] A total of 1823 patients who received pertussis nucleic acid detection and CBC in our hospital from June 1, 2023, to May 31, 2024, were enrolled. The inclusion criteria included: (1) Patients who received nucleic acid detection of Bordetella pertussis; (2) Patients who have not received antibacterial drugs or any other medications since the onset of symptoms; (3) Blood routine test and C-reactive protein were completed after the visit. The exclusion criteria were: (1) Patients with visceral dysfunction or tuberculosis, pneumonia, lung cancer and other pulmonary lesions; (2) Patients with severe infectious diseases, autoimmune diseases, congenital diseases, or malignant tumors; (3) Patients with a history of diarrhea or related drug use within two weeks. According to the inclusion and exclusion criteria, 538 patients with positive nucleic acid detection results of Bordetella

pertussis were assigned to the pertussis group, while 595 patients with negative nucleic acid detection results were placed in the control group.

Pertussis Nucleic Acid Detection

The Natch CS2 fully automated nucleic acid extraction system and Bordetella pertussis nucleic acid detection kit were purchased from Sansure Biotech Inc. The ABI 7500 real-time fluorescence quantitative PCR instrument was supplied by Applied Biosystems (USA). DNA was extracted for subsequent detection using nasopharyngeal swabs, according to the instructions in the nucleic acid extraction kit. Following the guidelines of the detection kit, the reaction system was prepared and the reaction conditions were set to perform PCR detection on the samples. The results were assessed according to the kit directions. A positive Bordetella pertussis sample can be declared when the positive and negative controls are under control, the FAM fluorescence (Bordetella pertussis) cycle threshold (Ct) value of the tested sample is ≤ 38.00, and there is a typical S amplification curve. Conversely, a negative sample can be judged when the FAM fluorescence (Bordetella pertussis) of the sample has no Ct value, the Ct value is > 38.00, or there is no typical S-type amplification curve.

Complete Blood Count and CRP

At the time of presentation, WBC count and CRP test were performed in all the patients. The CBC and CRP were performed using the BC-7500 CS automatic blood cell analyzer (Mindray, Shenzhen, China) and matching reagents. The background test and indoor quality control were conducted before daily use, and these reagents were used after being verified through relevant tests. The BC-7500 CS analyzer was inspected through external quality assessments of the National Center for Clinical Laboratories and the Zhejiang Center for Clinical Laboratories, and it achieved excellent results in both assessments. The on-machine testing was performed in strict accordance with the instructions of each instrument.

Statistical Analysis

SPSS 26.0 was used for data processing and the normality test was performed to assess relevant data. Non-normally distributed data were presented as a median (M) [interquartile (P25 - P75)]. The non-parametric Mann–Whitney *U*-test was conducted for comparisons between the two groups. The chi-square test was used to analyze the rate, while logistic regression analysis was applied for the regression analysis. $P < 0.05$ indicated that the difference was statistically significant.

Results

Pertussis Prevalence Over the Past ten Years

According to the data released by the WHO and the Health Commission of Zhejiang Province, the number of reported pertussis patients around the world exhibited a downward trend from 2014 to 2021. In particular, a relatively steep decline was reported after 2018. However, there was an increase in the number of pertussis patients in 2022, while the 2023 data were unavailable. The number of reported pertussis patients in China exhibited an upward trend from 2014 to 2019, although it fell considerably in 2020 and 2021. However, this value increased substantially in 2022 and 2023. The trends in the number of pertussis patients in Zhejiang province were largely consistent with that in China (Figure 1).

Monthly Pertussis Prevalence in Zhejiang Province from 2019 to 2023

The lowest number of pertussis patients was reported in 2020, and there was a negligible difference between the months of that year. In 2021 and 2023, the number of pertussis patients showed a gradual increase from January to December. A more significant increase was observed from October to December, especially in 2023. The largest number of pertussis patients was reported in 2022, exhibiting an inverted "V" shape and reaching its peak in June. In 2019, the number of pertussis patients first increased and then decreased, reaching a peak in May and then presenting a slow downward trend (Figure 2).

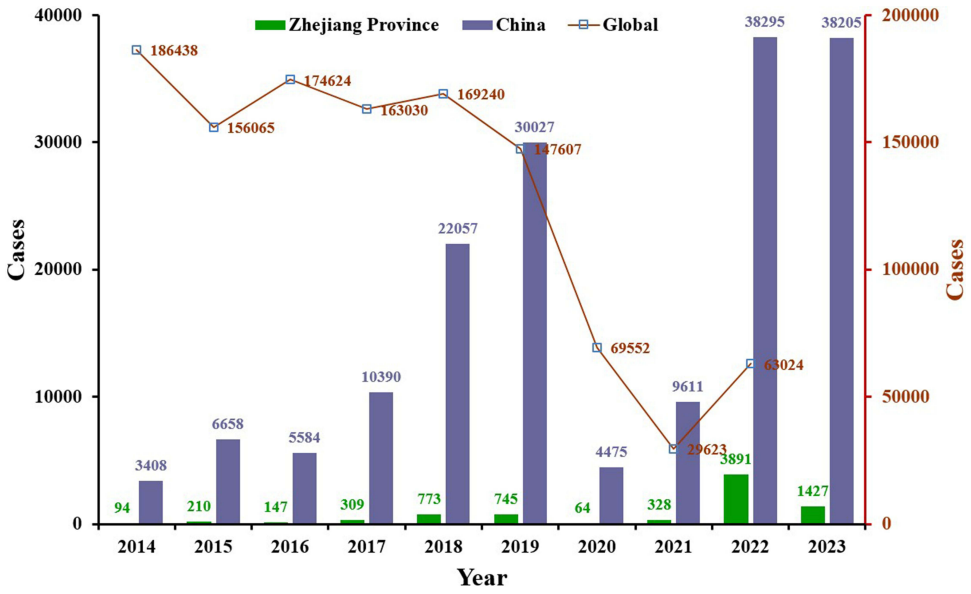

Figure 1 Number of reported pertussis patients by year of onset from 2014 to 2023.

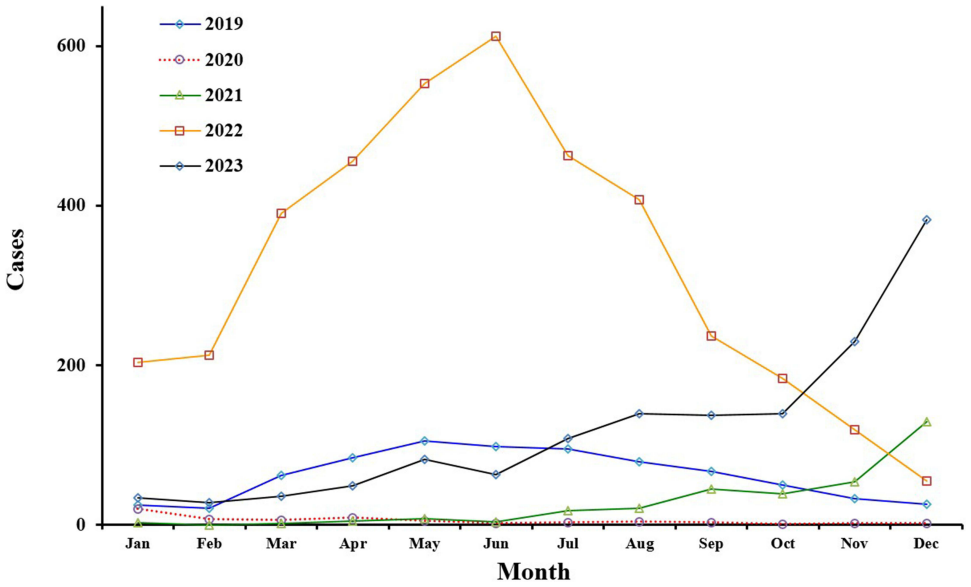

Figure 2 Number of reported pertussis patients by month of onset in Zhejiang province from 2019 to 2023.

Number of Pertussis Patients from June 2023 to May 2024

Between June 2023 and May 2024, the number of reported pertussis patients in China showed a rising trend, with greater numbers observed in 2024 and the largest increase occurring in April 2024. The trends regarding the number of pertussis patients in our hospital and Zhejiang province were essentially the same as those across China, with the largest numbers reported in April 2024 (Figure 3).

Distribution of Patients with Pertussis

From 2018 to 2020, the number of pertussis cases in China gradually decreased with age. Within this time, the number of infants under the age of 1 year with pertussis accounted for more than 50% of all patients. However, from June 2023 to May 2024, the proportion of children under the age of 5 with pertussis was extremely low, while the highest proportions were observed in children aged 6–7 years and 7–8 years (Figure 4).

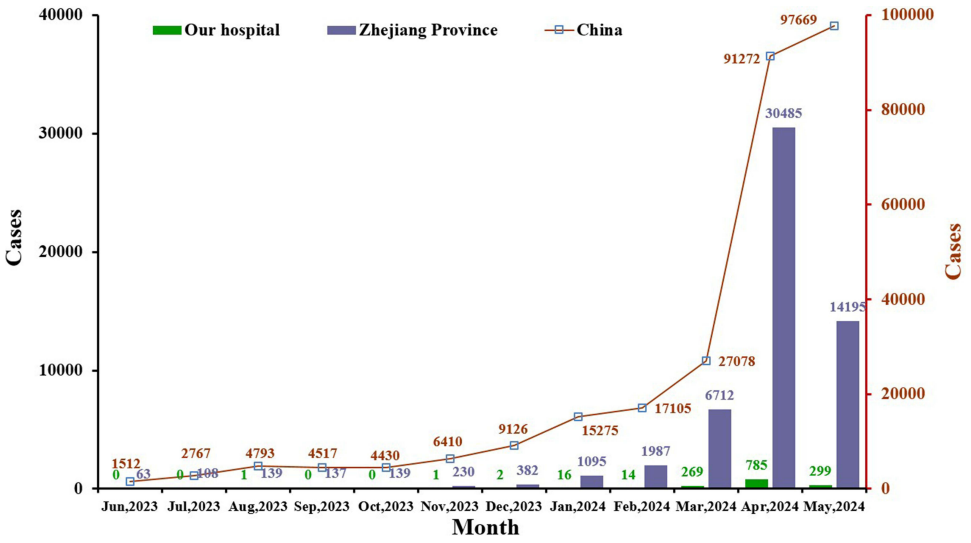

Figure 3 Number of reported pertussis patients by month of onset from June 2023 to May 2024.

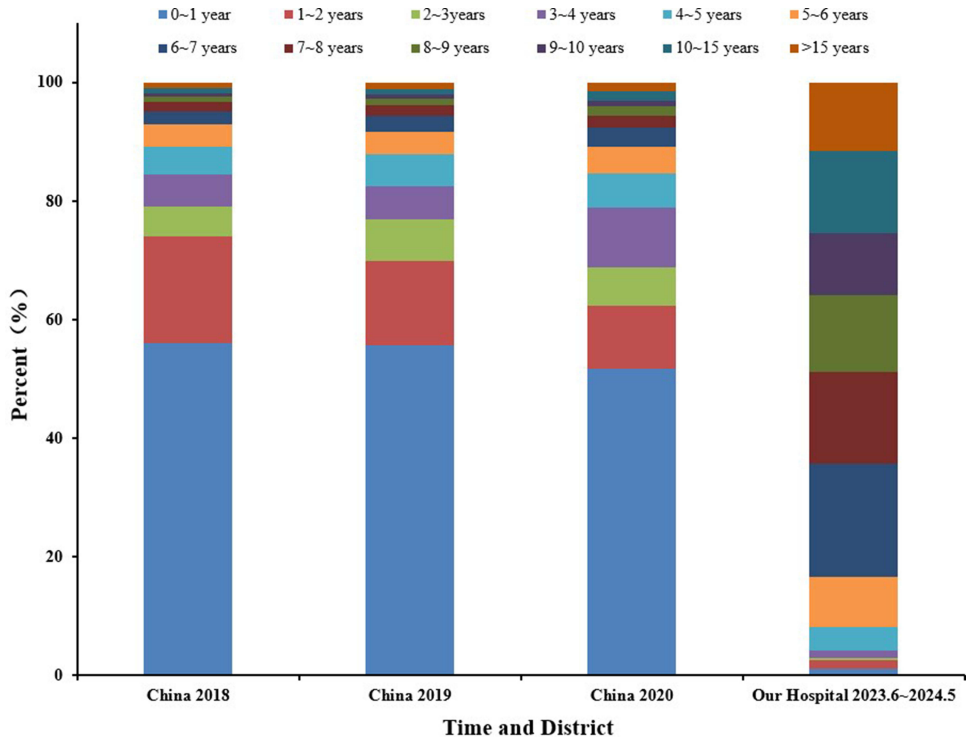

Figure 4 Distribution of pertussis patients with different ages.

CBC results in Patients with Pertussis

There was a negligible difference between the pertussis group and the control group in terms of gender, age, and other general data (P>0.05). However, the white blood count (WBC), lymphocyte percentage were higher, and platelet count (PLT) values was lower in the pertussis group than in the control group, and the differences were statistically significant (P<0.05). There was no statistical difference in C-reactive protein (CRP) between the two groups (P>0.05). The result is shown in Table 1.

Table 1 Comparison of the General Data, WBC, Lymphocyte, PLT, and CRP Between the Two Groups

Item		Pertussis Group	Control Group	Statistical Value	P-value
Cases		538	595	—	—
Gender	Male	246	279	−0.393	0.694
	Female	292	316		
Initial clinical diagnosis	Fever	42	55	−0.523	0.601
	Acute Bronchitis	307	329		
	Acute upper respiratory tract infection	144	150		
	Cough	28	38		
	Other	17	23		
Age (years)		7 (6–10)	7 (6–10)	−1.179	0.239
WBC ($\times 10^9$/L)		9.0 (7.2–11.2)	8.2 (6.6–10.2)	−4.699	<0.001
Lymphocyte proportion (%)		36.6 (29.08–44.4)	33.3 (24.7–42.5)	−3.465	0.001
PLT ($\times 10^9$/L)		288 (246–334)	298 (248–336)	−2.535	0.011
CRP (mg/L)		1.3 (0.5-3.8)	1.2 (0.5–3.5)	-1.375	0.175

Abbreviations: WBC, White blood count; PLT, Platelet; CRP, C-reactive protein.

Analysis of Diagnostic Indicators for Pertussis

The dependent variable was selected as a positive pertussis diagnosis and was based on the pertussis nucleic acid detection results (No = 0, Yes = 1). Additionally, age, gender, WBC, lymphocyte percentage, and PLT were selected as independent variables. On that basis, a logistic regression equation was established. The results revealed that elevated white blood cell counts, increased lymphocyte percentages, and abnormal platelet counts are correlated to some extent with pertussis infection. According to the odds ratio values, patients with high WBC, high lymphocyte percentage, and low PLT were more susceptible to pertussis (Table 2).

Positive WBC Rate and Lymphocyte Percentage in Patients with Pertussis

Of the 538 patients with pertussis, the lowest WBC value was 2.2×10^9/L, while the highest was 26.9×10^9/L. Moreover, 206 (38.29%) of the pertussis patients had a WBC value higher than the upper limit of the reference range. The lowest WBC of the 595 patients without pertussis was 2.8×10^9/L, while the highest was 28.4×10^9/L. Among these patients, 154 (25.88%) had a WBC value that exceeded the reference range upper limit. The lymphocyte percentage positivity rates in the pertussis group and the control group were 31.41% and 23.19%, respectively. The combined positivity rate of WBC

Table 2 Logistic Regression Results

Variable	B	SE	Wald	OR (95% CI)	P-value
Gender*	−0.194	0.106	3.335	0.824 (0.669–1.014)	0.068
Age (years)	0.004	0.004	0.929	1.004 (0.996–1.012)	0.335
WBC ($\times 10^9$/L)	0.095	0.019	24.537	1.100 (1.059–1.142)	<0.001
Lymphocyte percentage (%)	0.016	0.005	12.577	1.016 (1.007–1.026)	<0.001
PLT ($\times 10^9$/L)	−0.002	0.001	5.947	0.998 (0.997–1.000)	0.015

Note: *Female as the control group.

Table 3 Diagnostic Efficacy of the WBC and Lymphocyte Percentage

Item		Pertussis Group (n/%)	Control Group (n/%)	χ^2 value	P-value	Sensitivity	Specificity	Youden's Index
WBC ($\times 10^9$/L)	Not larger than the upper limit of the reference range	332/61.71	441/74.12	20.064	<0.001	38.29	74.12	0.124
	Larger than the upper limit of the reference range	206/38.29	154/25.88					
Lymphocyte percentage (%)	Within the limits of the reference range	369/68.59	457/76.81	9.662	0.002	31.41	76.81	0.082
	Larger than the upper limit of the reference range	169/31.41	138/23.19					
Combination of WBC and lymphocyte percentage	WBC and lymphocyte percentage are not both larger than the upper limit of their reference ranges	498/92.56	577/96.97	11.311	0.001	7.43	96.97	0.044
	Both WBC and lymphocyte percentage are larger than the upper limit of their reference ranges	40/7.44	18/3.03					

Notes: The reference range for the lymphocyte percentage in our hospital: 0–7 days: 0%-60.0%; 8 days - 1 year: 0%-70.0%; older than 1 year - 5 years: 5.0%-50.0%; > 5 years: 0%-40.0%. The reference range for WBC in our hospital: 0–7 days: 15.0–20.0×10^9/L; 8 days - 1 year: 4.0–12.0×10^9/L; older than 1 year - 5 years: 4.0–10.0×10^9/L; >5 years: 3.5–10.0×10^9/L.

and lymphocyte percentage was 7.44% in the pertussis group and 3.03% in the control group. The differences in the positivity rates for WBC, lymphocyte percentage, and their combination between the two groups were statistically significant ($P < 0.05$), with Youden's index values of 0.124, 0.082, and 0.044, respectively (Table 3).

Discussion

Despite the widespread implementation of vaccinations over the past three decades, pertussis remains a public health challenge that cannot be ignored. For patients with suspected pertussis, PCR detection has gradually become the principal tool for diagnosis confirmation, as an alternative to culture methods.[17] Besides, the recent COVID-19 pandemic and other factors may also have contributed to changes in pertussis epidemiology. Thus, it is necessary to conduct systematic analyses of the epidemiological characteristics of pertussis in China and the diagnostic efficacy of various diagnostic indicators. This holds important scientific significance and practical value for formulating prevention and control strategies and optimizing the diagnosis and treatment regimens of pertussis.

In this study, we discovered that the global incidence of pertussis first decreased and then increased in the last decade. In contrast, it first rose, then fell, and then rose again in both China and Zhejiang province, with the peak base occurring in 2020 and 2021. He et al adopted the serum antibody determination method to explore the prevalence of pertussis and confirmed that the incidence rate of pertussis decreased in China during the COVID-19 pandemic.[18] Seroepidemiological results regarding research on pertussis in eastern China by Chen et al also revealed that the incidence of pertussis after the COVID-19 pandemic was higher than before the pandemic.[19] However, Sandoval reported that the number of patients with pertussis fell dramatically after the outbreak of the COVID-19 pandemic.[20] The findings of this study are consistent with other papers that utilize different approaches and may be related to the COVID-19 pandemic. During the COVID-19 pandemic, humans drastically changed their attitudes and practices toward the prevention and control of infectious diseases, significantly promoting the innovation and application of pathogen detection technology. Additionally, diseases

caused by respiratory infections were also effectively prevented due to the implementation of a series of stringent non-pharmaceutical interventions, such as lockdowns, mask-wearing, and social distancing.[21,22]

A monthly analysis of pertussis incidence in Zhejiang province over the past five years (2019–2023) did not reveal any seasonal patterns. Moreover, the incidence of pertussis in China, Zhejiang province, and our hospital in the past year (from June 2023 to May 2024) exhibited an upward trend, peaking in April 2024. However, Feng et al noted that most patients with pertussis were reported in spring and summer, with peaks in July and August.[2] Zhang et al conducted a study on the epidemiological characteristics of pertussis in China in 2022. Their results indicated that the number of patients with pertussis was relatively high between May and August, with a peak observed in August.[23] The results of our study were quite dissimilar and may be related to multiple factors such as location, natural environment, and outbreaks of different pathogens. From 2018 to 2020, pertussis was most prevalent in infants under the age of 1 year in China, accounting for more than 50% of all patients with pertussis. However, between June 2023 and May 2024, pertussis in infants under the age of 1 year accounted for only 1.12% of all pertussis patients in our hospital, which was far lower than in the whole country in previous years. In the same period, the proportion of patients with pertussis over the age of 5 reached 91.82%, which was radically different from previous findings that stated pertussis was most widespread in infants and young children. However, our results were consistent with a European Union report in 2018 that revealed the number of patients with pertussis aged ≥ 15 years accounted for 62% of all pertussis patients. Additionally, our findings were similar to those that appeared in an analysis of reported pertussis cases based on laboratory results and clinical diagnoses by the Chinese Disease Prevention and Control Information System, which revealed that the number of pertussis patients aged 5–9 had risen to the second place among all age groups.[24,25] Since our study was designed as a single-center small-sample study based on a local population, our results may be biased to a certain extent. Consequently, pertussis may be prevented and controlled by improving the immunity of all ages and implementing immunization boosters for school-age children, adolescents, and adults. This approach may reduce the risk of disease or transmission to infants and young children.

As one of the most common clinical examinations, CBC can be implemented in almost all medical institutions. According to *Diagnosis and Treatment Plan for Pertussis* (2023) and *Guidelines for Diagnosis and Management and Prevention of Pertussis of China* (2024), both increased WBC and higher lymphocyte percentage in CBC are recommended as auxiliary diagnostic indicators for pertussis, but their diagnostic value has not been verified.[5,10] In this study, we found that there were indeed some differences in the WBC, lymphocyte percentage, and PLT in CBC between pertussis and non-pertussis patients. Additionally, a logistic analysis was performed on all patients who had simultaneously completed Bordetella pertussis nucleic acid detection and the CBC test in our hospital within one year. The results revealed that elevated WBC, increased lymphocyte percentage, and abnormal PLT are correlated with pertussis infection. However, their OR values were close to 1, suggesting a weak influence. Moreover, the diagnostic capability of WBC and lymphocyte percentage was also analyzed in this paper. The Youden's index of WBC and lymphocyte percentage both alone and in combination (in a sequential pattern) was lower than 0.15, indicating that the diagnostic efficacy of the two indicators was poor. The WBC and lymphocyte percentage were only 38.29% and 31.41%, respectively, implying that many pertussis patients could experience missed diagnoses based on these two indicators. Therefore, CBC should only be used as an auxiliary indicator of pertussis. The final diagnosis of this disease should be based on a combination of clinical symptoms, medical history, and more specific tests, such as Bordetella pertussis nucleic acid detection, serological antibody detection, or Bordetella pertussis culture.

Dong et al showed that the WBC and lymphocyte ratio in pertussis patients are also elevated, and the results of this study are basically consistent with findings reported by Xu Dong.[26] Additionally, Hui et al showed that severe pertussis patients have a higher white blood cell count and a higher mortality rate.[27] These studies suggest that blood routine indicators can assist in the diagnosis and treatment of pertussis, but are insufficient for definitive diagnosis or screening alone. This study analyzed the epidemiological data of pertussis over the past five years and explored the value of blood routine as a diagnostic indicator. However, this study also has some limitations, mainly that it is a single-center study with a limited sample size, which may not fully reflect the overall epidemiological characteristics. Furthermore, although blood routine is a convenient diagnostic tool, its diagnostic efficacy in this study was relatively low, indicating that its effectiveness as an independent screening tool is limited.

Conclusions

The incidence of pertussis is on the rise as a whole, although the number of patients with pertussis was relatively small during the COVID-19 pandemic. Although gender and age are not risk factors for pertussis, the number and proportion of adolescents and adults with pertussis have increased sharply. Therefore, it is necessary to optimize immunization strategies to protect susceptible populations. The results revealed that elevated WBC, increased lymphocyte percentage, and abnormal PLT are correlated with pertussis infection. However, the WBC and lymphocyte percentage of most patients were within the normal reference range, indicating that their influence was insubstantial. The WBC and lymphocyte percentage alone, as well as the two combined, were not potent enough to effectively diagnose this disease. It is inappropriate to apply only the WBC and lymphocyte percentage in the screening of pertussis, and both indicators should only be used as auxiliary diagnostic indicators. This research revealed new trends in pertussis epidemiology, particularly the rising proportion of adult patients, indicating a need for future studies to investigate the underlying causes and mechanisms of this trend, and to reassess current immunization strategies.

Data Sharing Statement

We declared that materials described in the manuscript, including all relevant raw data, will be freely available to any scientist wishing to use them for non-commercial purposes, without breaching participant confidentiality.

Ethics Approval and Consent to Participate

This study was conducted with approval from the Ethics Committee of First People's Hospital of Linping District, Hangzhou (No. 2023043). This study was conducted in accordance with the declaration of Helsinki. Written informed consent was obtained from all participants.

Consent for Publication

The study described is original research that has not been published previously, and is not under consideration for publication elsewhere, in whole or in part.

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Disclosure

The authors declare that they have no competing interests.

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