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ORIGINAL RESEARCH

# Trends and Characteristics of Pertussis Epidemic in Pediatric Patients During and After the COVID-19 Pandemic in East China

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**Background:** Pertussis is a highly contagious respiratory disease caused by Bordetella pertussis, posing a significant health threat to children. Despite vaccination efforts, a resurgence of pertussis has been observed globally, especially during and after the COVID-19 pandemic. This study aims to investigate the epidemiological trends and characteristics of pertussis among pediatric patients during and after the COVID-19 pandemic in East China.

**Methods:** We included 92,300 patients aged 0–18 years with suspected symptoms of pertussis infection from January 1, 2022, to November 30, 2024, in a tertiary children's hospital in China. Clinical information (eg, detection date, date of birth, gender, type of patients) and pertussis test results were extracted from the laboratory information system. We used two independent sample *t*-tests and Chi-square tests to compare differences in the above-mentioned variables between the two pandemic phases. Positive detection rates were calculated across age groups, gender, patient types, seasons, and pandemic phases, while nonlinear associations between age and detection rates were assessed using restricted cubic spline regression models.

**Results:** Twenty-two thousand six hundred and forty-two (24.5%) cases were detected as positive cases. Cases surged from November 2023, peaking in April 2024 (n=5363). The highest positive detection rate of pertussis infection was observed in children aged over 6 years (36.2%), particularly among outpatients (37.6%), while the lowest rate was in those aged 18 months to 3 years (12.8%); significant differences were also noted by gender, patient type, season, and COVID-19 pandemic phases ($p < 0.05$). Nonlinear regression analysis shows a higher risk and wider susceptible age range after the COVID-19 pandemic than those during the pandemic ($p_{\text{non-linear}} < 0.001$).

**Conclusion:** This study highlights the resurgence of pertussis among children in Eastern China during and after the COVID-19 pandemic, emphasizing significant epidemiological shifts and expanded age susceptibility, underscoring the urgent need for enhanced vaccination strategies and public health interventions.

**Keywords:** pertussis, resurgence, epidemiology, children, COVID-19 pandemic

## Introduction

Pertussis, or whooping cough, is a highly contagious acute respiratory tract infection caused by the gram-negative obligate human pathogen *Bordetella pertussis (Bp)*. Worldwide, pertussis remains a serious health concern. The disease is primarily spread through droplets produced during coughing or sneezing.[1] Initial symptoms resemble those of a common cold, such as cough, runny nose, and fever, which typically progress to a severe cough followed by a distinctive whooping sound after one to two weeks of onset.[2] Pertussis is highly communicable, especially in a household. The general population is commonly susceptible to *Bordetella pertussis*, with infants and young children being at



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a heightened risk of developing the disease. Specifically, infants under the age of two months have been documented to experience the highest rates of incidence and mortality.[3] Globally, it is estimated that there were 24.1 million pertussis cases and 160,700 deaths in children under 5 years of age in 2014.[4]

Pertussis is a disease that can be prevented through vaccination. Since the 1950s, whole-cell pertussis vaccines were developed and implemented in Western countries, achieving near-global utilization by the 1970s.[5] Nonetheless, concerns regarding neurological and other adverse reactions in children following the administration of whole-cell pertussis vaccines have led to the gradual replacement of these vaccines with acellular pertussis vaccines in recent years. The World Health Organization (WHO) recommends that all countries aim to initiate early and timely vaccination starting at 6 weeks of age and no later than 8 weeks while maintaining a high coverage rate of at least 90% with a minimum of three doses of a quality-assured pertussis vaccine at both national and subnational levels. In China, according to the National Immunization Program (NIP), three doses of Diphtheria Pertussis tetanus (DPT) vaccines are administered at three, four and six months after birth.

Despite the high global vaccine coverage, pertussis is experiencing a resurgence worldwide, particularly among young children.[6] Over the past decade, the incidence of reported pertussis cases has been increasing in countries such as the United States, Canada, and the United Kingdom.[7,8] In China, the incidence of pertussis remained relatively low from 2006 to 2013. However, a marked increase was observed beginning in 2014, culminating in 30,027 cases by 2019.[9] In 2020, the number of pertussis cases experienced a rapid decline, followed by a notable rise from 2021 to 2023. Since the onset of 2024, there has been a significant escalation in both the incidence and mortality rates associated with pertussis. According to the most recent data published by the Chinese National Disease Control and Prevention Administration, there were 452,396 reported cases of pertussis nationwide from January to August 2024.[10] This number signifies an eleven-fold increase compared to the total number of cases documented for the entire year of 2023, which was 41,124.[11] The resurgence of pertussis among Chinese children in 2024 likely resulted from waning vaccine immunity, bacterial adaptation, asymptomatical adult carriers, increased social contact post-pandemic, and natural epidemic cycles.[12,13]

The resurgence of pertussis has raised serious public health concerns and coincides with the onset of COVID-19 and the implementation of stringent preventive and control measures in China. It is hypothesized that this may be attributable to interruptions to routine vaccination schedules, limited access to healthcare, and shifts in social interactions during this period, which have likely heightened the risk of pertussis transmission, particularly among children, worsening the issue of "immunity debt" due to missed immunizations and lower exposure to pathogens.[12] Regarding the unintended ecological impact of the COVID-19 pandemic on pertussis epidemic, data remains limited. This intricate situation highlights the urgent need for focused epidemiological research to better understand and tackle these growing challenges. Therefore, the present study used data extracted from a laboratory information system of a tertiary children's hospital in Zhejiang Province, China, aiming to evaluate the trends and characteristics of pertussis epidemic in children during and post COVID-19 pandemic in East China.

# Methods

## Study Population

The study included all patients meeting the following inclusion criteria:

1. Patients aged younger than 18 years;
2. Patients visited Children's Hospital of Zhejiang University School of Medicine from January 1, 2022, to November 30, 2024;
3. Patients with suspected pertussis infection may present with respiratory symptoms like coughing (with or without fever) or running nose.

Exclusion criteria:

1. Patients aged 18 years or older at the time of testing.
2. Incomplete or missing medical records critical for analysis (eg, test results, demographic data).
3. Confirmed alternative diagnoses unrelated to pertussis (eg, other respiratory infections).

If a child had multiple tests of pertussis during the course of disease, only the result of first test was included.

The study was conducted according to the Declaration of Helsinki,[14] and was approved by the medical ethics committee of Children's Hospital, Zhejiang University School of Medicine (No. 2024-IRB-0117-P-01). As the data utilized in this study were obtained from the hospital's electronic laboratory information system and no additional physical harm was inflicted upon the participants, the Medical Ethics Committee granted a waiver for informed consent.

## Data Collection

Respiratory specimens (nasopharyngeal swab) were collected from all of the enrolled patients by trained medical staff following standard operating procedures. Samples were stored at 4°C for no more than 48 hours until being tested. *Bordetella pertussis* nucleic acid was tested by a diagnostic kit (Polymerase Chain Reaction-fluorescent probe method) (Sansure Biotech Inc). It uses the conserved sequence of *B. pertussis* as the target region and designs specific primers and probes. The fluorescence quantitative PCR instrument utilizes real-time fluorescence detection to detect *B. pertussis* DNA through changes in fluorescence signals. The kit was approved by the National Medical Products Administration (NMPA) of China (Approval No. 20223401564).

Clinical information was extracted from the laboratory information system of Children's Hospital, Zhejiang University School of Medicine, including age, gender, patient type (inpatients/outpatients), sample collection date, and detection result of pertussis (positive/negative). Six age groups (0–3 months, 3–6 months, 6–18 months, 18 months–3 years, 3–6 years, and > 6 years) were determined based on clinical experience, reflecting key developmental stages, immune response variations, and pertussis vaccination schedules relevant to disease susceptibility and severity in pediatric populations. Seasons were categorized based on the sample collection date, that is, spring (March–May), summer (June–August), autumn (September–November), and winter (December–February). According to the administration of COVID-19 pandemic in China, we defined two phases. Phase I was defined as "during COVID-19 pandemic", referring to the dates between January 1, 2022, and December 18, 2022; and Phase II was defined "post COVID-19 pandemic", referring to the period after the date of December 19, 2022, when the Zhejiang Province began to ease most COVID-19 restrictive measures.

## Statistical Analyses

Firstly, we conducted the descriptive analysis to present the general and clinical characteristics of the study population. The normality of the continuous variable was tested, ie, age in our study, which exhibited a normal distribution, and we reported the mean and standard deviation. Categorical variables were presented as numbers and percentages. Furthermore, we compared the difference in the proportion of above-mentioned general and clinical variables between during and post- COVID-19 pandemic. The two-independent sample *t*-tests was employed for the continuous variable, while the Chi-square tests were used for categorical variables. Secondly, we calculated the positive detection rates of pertussis and its 95% confidence intervals (CI) for all patients and for each age subgroup classified by gender, patient types, seasons, and COVID-19 pandemic phases. In addition, we calculated positive rates across age groups by gender, patient types and seasons in Phase I and II, respectively. Lastly, the nonlinear association between age and positive detection rate at each pandemic phase was assessed by the restricted cubic spline regression model with three knots at the 25th, 50th, and 75th percentiles.

All statistical analyses were conducted using the R software program (version 4.4.1). The statistical significance is indicated when $p$ value < 0.05 (two tails).

# Results

## General and Clinical Characteristics of the Study Population

Table 1 presents the general and clinical characteristics of the study population. Among 92,300 patients included for analyses, 11,189 (12.1%) patients visited the hospital during COVID-19 pandemic, and 81,111 (87.9%) after the pandemic. The mean age of the study population was 5.7 years; patients were significantly younger in Phase II compared with those in Phase I (5.5 vs 7.1, p< 0.001). About 44.4% of patients were older than 6 years; 53.0% were boys; 90.7% were outpatients; and 48.9% were tested in spring. There were statistically significant differences between two pandemic

**Table 1** General and Clinical Characteristics of the Study Population[a]

| Variables | Overall (n = 92,300) | Phase I (n = 11,189) | Phase II (n = 81,111) | Statistic | *p* value |
|---|---|---|---|---|---|
| Age, mean (SD) | 5.7 (3.3) | 7.1 (3.2) | 5.5 (3.2) | $t = 49.4$ | < 0.001 |
| Age group, n(%) | | | | $\chi^2 = 2139.2$ | < 0.001 |
| 0–3 months | 574 (0.6) | 0 (0.0) | 574 (0.7) | | |
| 3–6 months | 1912 (2.1) | 0 (0.0) | 1912 (2.4) | | |
| 6–18 months | 7870 (8.5) | 24 (0.2) | 7846 (9.7) | | |
| 18 months–3 years | 9983 (10.8) | 1447 (12.9) | 8536 (10.5) | | |
| 3–6 years | 30,987 (33.6) | 3138 (28.0) | 27,849 (34.3) | | |
| > 6 years | 40,974 (44.4) | 6580 (58.8) | 34,394 (42.4) | | |
| Gender, n(%) | | | | $\chi^2=0.1$ | 0.78 |
| Boy | 48,917 (53.0) | 5944 (53.1) | 42,973 (53.0) | | |
| Girl | 43,383 (47.0) | 5245 (46.9) | 38,138 (47.0) | | |
| Type of patients, n(%) | | | | $\chi^2=391.5$ | < 0.001 |
| Outpatient | 83,757 (90.7) | 10,722 (95.8) | 73,035 (90.0) | | |
| Inpatient | 8,543 (9.3) | 467 (4.2) | 8076 (10.0) | | |
| Season, n(%) | | | | $\chi^2=1550.2$ | < 0.001 |
| Spring | 45,108 (48.9) | 3636 (32.5) | 41,472 (51.1) | | |
| Summer | 27,684 (30.0) | 4395 (39.3) | 23,289 (28.7) | | |
| Autumn | 12,953 (14.0) | 2388 (21.3) | 10,565 (13.0) | | |
| Winter | 6555 (7.1) | 770 (6.9) | 5785 (7.1) | | |

**Note**: [a]Values presented in this table are means, standard deviations, numbers, percentages, statistics and *p* values.

phases in terms of age groups, type of patients and seasons (all $p$ values < 0.001); no gender difference was observed ($p$ value = 0.78). Additionally, seasonal variations among participants were further analyzed and provided in Supplementary Table S1.

Figure 1 illustrates the number of positive pertussis cases in both outpatients and inpatients who received the pertussis test at the Children's Hospital, Zhejiang University School of Medicine, from January 1, 2022, to November 30, 2024. The exact numbers of positive cases of pertussis were presented in the Supplementary Table S2. In total, 22,642 (24.5%) cases were detected with pertussis infection among 92,300 patients. In 2022, the number was 2536; it decreased to 571 in 2023; and raised up dramatically to 19,535 by 30 November 2024. More specifically, an upward trend in positive cases was observed beginning in January 2022, culminating in a peak in June 2022, followed by a subsequent decline. Throughout 2023, the number of positive cases remained consistently low. Afterwards, a significant increase was noted starting in November 2023, reaching a peak in April 2024 (n = 5363). Subsequently, we observed a month-on-month decline in positive cases from May 2024 onwards. The trends of positive pertussis cases are almost the same in outpatients and inpatients.

## Positive Detection Rates of Pertussis Across Age Groups

Table 2 showed the positive detection rate of pertussis infection across age groups. Overall, the highest positive rate was observed in patients aged above six years, ie, 36.2%, while the lowest rate was in those aged 18 months – 3 years, ie, 12.8%. The positive rate was statistically significantly higher in girls than that in boys (25.3% vs 23.8%, $p < 0.001$) in the overall study population, and in subgroups of children aged 6 to 18 months and 18 months to 3 years ($p$ values ≤ 0.001). Outpatients had a higher overall positive detection rate than inpatients (25.9% vs 11.0%, $p < 0.001$) in the study population, and subgroups of children aged 6–18 months, 18 months – 3 years, 3–6 years and > 6 years ($p$ values < 0.05). Among them, the outpatient group of children older than 6 years had the highest positive detection rate (ie, 37.6%). Besides, there are also statistically significant differences in positive rates across seasons and phases of COVID-19 pandemic. More specifically, we presented the results of positive detection rates of pertussis infection across age groups by gender, patient type and season in two phases of COVID-19 pandemic separately in Supplementary Tables S3 and S4.

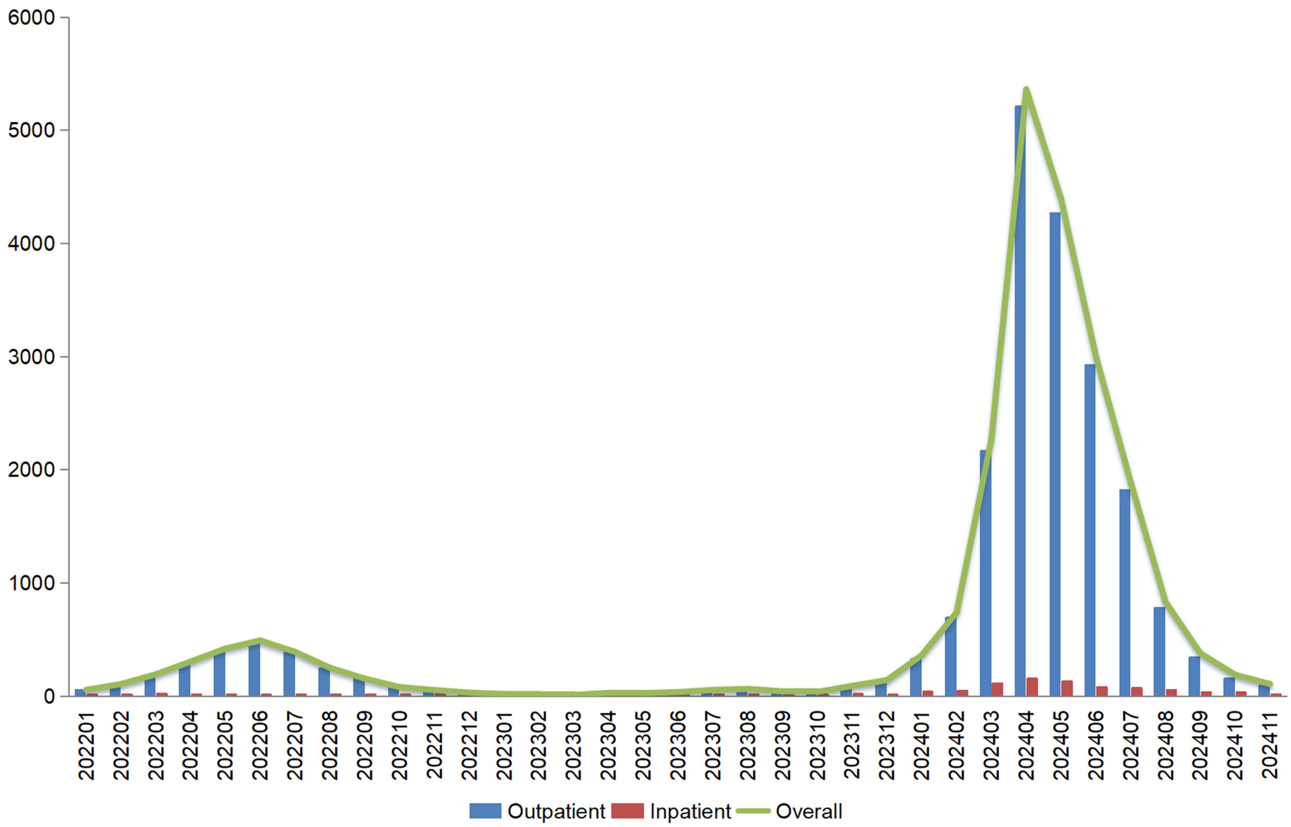


**Figure 1** Trends of pertussis cases from January, 2022 to November, 2024 in the study population.

## Comparison of Positive Detection Rates by Seasons and by Patient Types Across Age Groups Between Two Phases of the COVID-19 Pandemic

Figure 2 illustrates the positive detection rates of pertussis infection across age groups at Phase I and II of the COVID-19 pandemic. In Phase II, pertussis infection emerged in very young children aged 0–3 months and 3–6 months, and children aged > 6 years had the highest positive detection rate. In general, the detection rate is relatively higher at each age group in Phase II compared with that in Phase I, except for the age group of 18 months–3 years. In outpatients, positive pertussis cases were emerging in younger age groups, ie, 0–3 months, 3–6 months, and 6–18 months at Phase II, which was not observed in Phase I, and older children, ie, > 6 years, presented with highest positive detection rate (39.4%) in Phase II compared with rates in other age groups and with rates in Phase I. Among inpatients, positive pertussis cases were emerging in younger age groups, ie, 0–3 months and 3–6 months at Phase II, which was not observed in Phase I. Regarding the season, positive cases were emerging in younger age groups, ie, 0–3 months, 3–6 months, and 6–18 months in spring, summer and autumn at Phase II, while in 3–6 months and 6–18 months in winter, which was not observed in Phase I; and older children, ie, > 6 years, had the highest positive detection rates at each season in Phase II compared with rates in other age groups at Phase II.

## Projecting the Susceptible Age to Pertussis Infection in Phase I and Phase II Using the Restricted Cubic Spline Regression Model

Figure 3 presents a U-shape for the association between age and the positive detection rate of pertussis infection ($p_{non\text{-}linear} < 0.001$) in both Phase I and Phase II using the restricted cubic spline regression model. As projected by the piecewise logistic regression, the risk of having pertussis infection was higher at Phase II than that in Phase I, and the range of susceptible ages to pertussis infection was wider at Phase II than that in Phase I of the COVID-19 pandemic.

**Table 2** Positive Detection Rates and 95% Confidential Intervals of Pertussis Infection Across Age Groups

| | All Patients (n = 92,300) | 0 – 3 Months (n = 574) | 3 – 6 Months (n = 1912) | 6 – 18 Months (n = 7870) | 18 Months – 3 Years (n = 9983) | 3 – 6 Years (n = 30,987) | > 6 Years (n = 40,974) |
|---|---|---|---|---|---|---|---|
| Overall | 24.5 [24.2, 24.8] | 15.7 [12.8, 18.9] | 20.8 [19.0, 22.7] | 16.0 [15.2, 16.9] | 12.8 [12.1, 13.4] | 15.4 [15.0, 15.8] | 36.2 [35.8, 36.7] |
| Gender | | | | | | | |
| Boy | 23.8 [23.5, 24.2] | 13.2 [9.7, 17.4] | 20.0 [17.7, 22.5] | 14.8 [13.8, 15.9] | 11.7 [10.9, 12.6] | 15.3 [14.8, 15.9] | 35.9 [35.3, 36.6] |
| Girl | 25.3 [24.9, 25.7] | 18.9 [14.2, 24.3] | 21.8 [19.1, 24.8] | 17.7 [16.4, 19.1] | 14.2 [13.1, 15.2] | 15.5 [14.9, 16.1] | 36.5 [35.9, 37.2] |
| *p* value | < 0.001 | 0.08 | 0.36 | 0.001 | < 0.001 | 0.66 | 0.20 |
| Type of patients | | | | | | | |
| Outpatient | 25.9 [25.6, 26.2] | 20.0 [13.8, 27.4] | 20.5 [18.0, 23.1] | 16.5 [15.6, 17.5] | 13.4 [12.7, 14.1] | 16.1 [15.7, 16.6] | 37.6 [37.2, 38.1] |
| Inpatient | 11.0 [10.4, 11.7] | 14.2 [11.1, 17.9] | 21.2 [18.6, 24.0] | 14.5 [12.9, 16.1] | 8.7 [7.2, 10.3] | 4.1 [3.3, 5.1] | 10.4 [9.1, 11.7] |
| *p* value | < 0.001 | 0.13 | 0.74 | 0.03 | < 0.001 | < 0.001 | < 0.001 |
| Season | | | | | | | |
| Spring | 28.9 [28.4, 29.3] | 17.7 [13.5, 22.5] | 23.4 [20.7, 26.2] | 18.7 [17.4, 20.0] | 13.7 [12.8, 14.8] | 19.2 [18.5, 19.8] | 40.7 [40.1, 41.4] |
| Summer | 25.3 [24.8, 25.9] | 13.0 [4.9, 26.3] | 21.2 [17.6, 25.2] | 17.9 [16.3, 19.5] | 16.0 [14.6, 17.4] | 17.0 [16.2, 17.8] | 34.6 [33.8, 35.4] |
| Autumn | 8.8 [8.3, 9.3] | 13.7 [9.6, 18.8] | 14.9 [11.1, 19.3] | 7.4 [6.0, 8.9] | 5.3 [4.4, 6.4] | 4.6 [4.1, 5.1] | 18.4 [17.1, 19.8] |
| Winter | 22.5 [21.5, 23.5] | / | 17.3 [12.3, 23.4] | 11.9 [9.6, 14.4] | 13.9 [11.4, 16.8] | 14.5 [12.8, 16.2] | 30.8 [29.2, 32.4] |
| *p* value | < 0.001 | / | 0.008 | < 0.001 | < 0.001 | < 0.001 | < 0.001 |
| Pandemic phases | | | | | | | |
| Phase I | 22.6 [21.8, 23.4] | / | / | 12.5 [2.7, 32.4] | 22.9 [20.7, 25.1] | 9.6 [8.6, 10.6] | 28.8 [27.7, 29.9] |
| Phase II | 24.8 [24.5, 25.1] | 15.7 [12.8, 18.9] | 20.8 [19.0, 22.7] | 16.0 [15.2, 16.9] | 11.1 [10.4, 11.7] | 16.1 [15.7, 16.5] | 37.6 [37.1, 38.2] |
| *p* value | < 0.001 | / | / | /[a] | < 0.001 | < 0.001 | < 0.001 |

**Note**: [a]Due to the large difference in sample sizes between two groups, *p* value cannot be calculated.

## Discussion

The present study analyzed the data from 92,300 Chinese neonates, infants, children and adolescents suspected of pertussis infection, and described the trend and characteristics of pertussis epidemic among pediatric patients in East China from 2022 to 2024. We observed fluctuations in the numbers of pertussis cases. In particular, since early 2024, it dramatically increased and reached a peak in April with an alarming number, which indicated concerning trends and demanded for vigilant monitoring. Additionally, we compared the epidemiological characteristics between two phases of COVID-19 pandemic, ie, during and post the pandemic. Pertussis infection emerged in very young age groups such as 0–3 months, 3–6 months and 6–18 months in the post pandemic phase. The positive detection rate was highest in older children, ie, above 6 years, compared to that in other age groups, especially in the post pandemic phase.

In the current study sample, we observed a sharp increase in the number of pertussis cases after December 2023, reaching a peak in April, 2024 (n=5363). A violent pertussis outbreak since late 2023 is also a global trend. In the first half of 2024, the global incidence of pertussis surpassed the total number of cases reported throughout 2023.[15] For instance, there was an increase in pertussis cases in both Latin America and the United States during 2024. Specifically, in the United States, there was a 300% increase in cases within the first six months of 2024, amounting to 7251 reported cases.[15] European countries are also experiencing pertussis resurgence in 2024.[16] The Same trend was also reported worldwide, including in the UK, the Czech Republic, the Netherlands, and elsewhere. The resurgence of pertussis can be attributed to a multifaceted interplay of factors, including the periodic global outbreaks of the disease, advancements in diagnostic techniques, the waning immunity associated with acellular vaccine immunization, the pathogenic characteristics of *Bordetella pertussis*, the accumulation of susceptible populations, and the emergence of atypical cases that may serve as potential sources of infection for children, etc.[17] Pertussis exhibits epidemic cycles every three to five years, a pattern that remains unaltered despite high global vaccine coverage.[18] In response to modifications in vaccine manufacturing processes, China has adopted the use of co-purified acellular pertussis vaccines. These vaccines are associated with reduced adverse effects; however, they may also demonstrate diminished efficacy.[19] Specifically, the co-purified acellular pertussis vaccines implemented in China's national immunization program have been shown to induce lower levels of anti-pertussis toxin IgG compared to their separately purified acellular counterparts.[20]

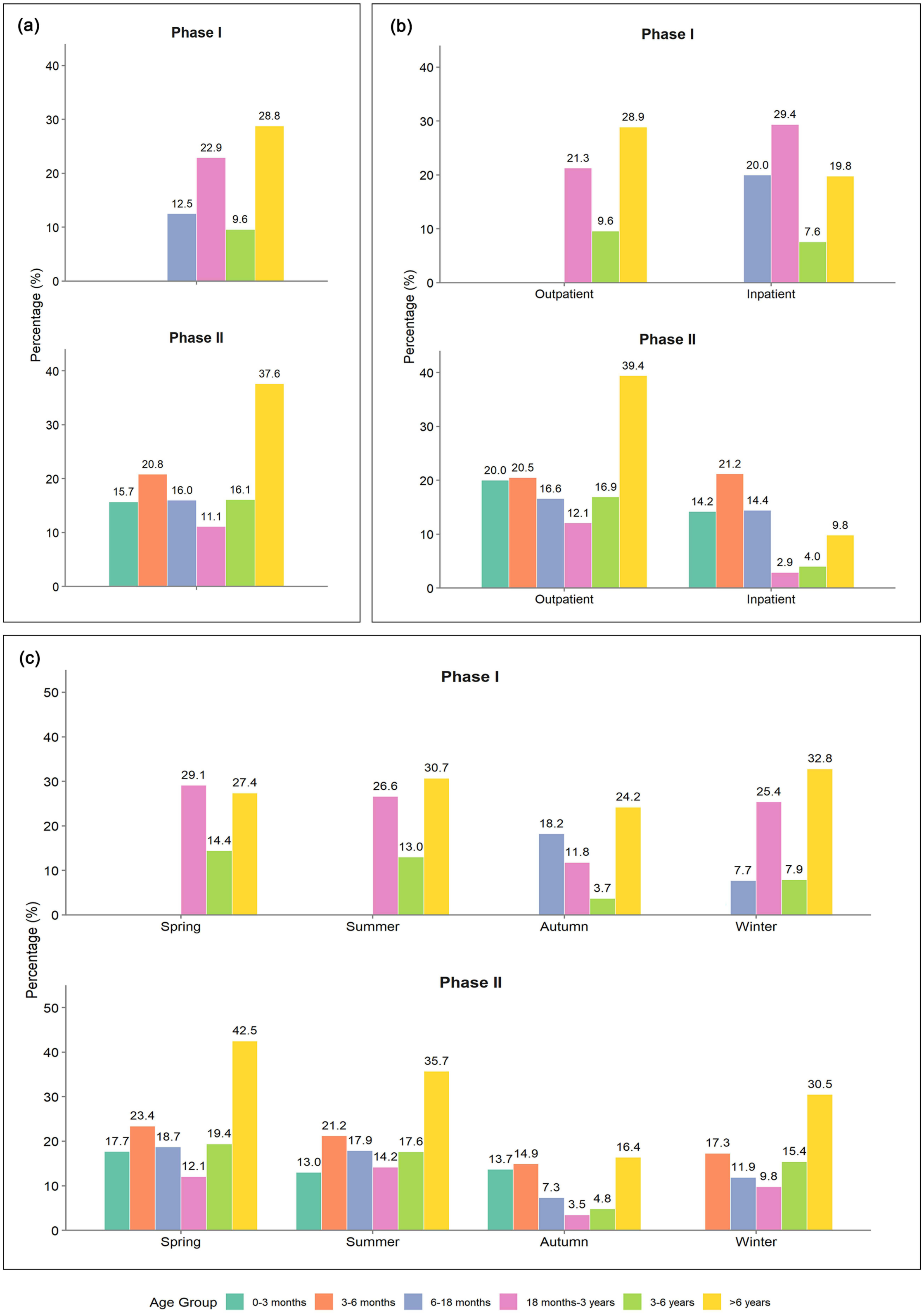


**Figure 2** Positive detection rates of pertussis infection by age groups. (**a**) Positive detection rates of pertussis infection by age groups in Phase I and II of COVID-19 pandemic; (**b**) Positive detection rates of pertussis infection by patient type and by age groups in Phase I and II of COVID-19 pandemic; (**c**) Positive detection rates of pertussis infection by season and by age groups in Phase I and II of COVID-19 pandemic.

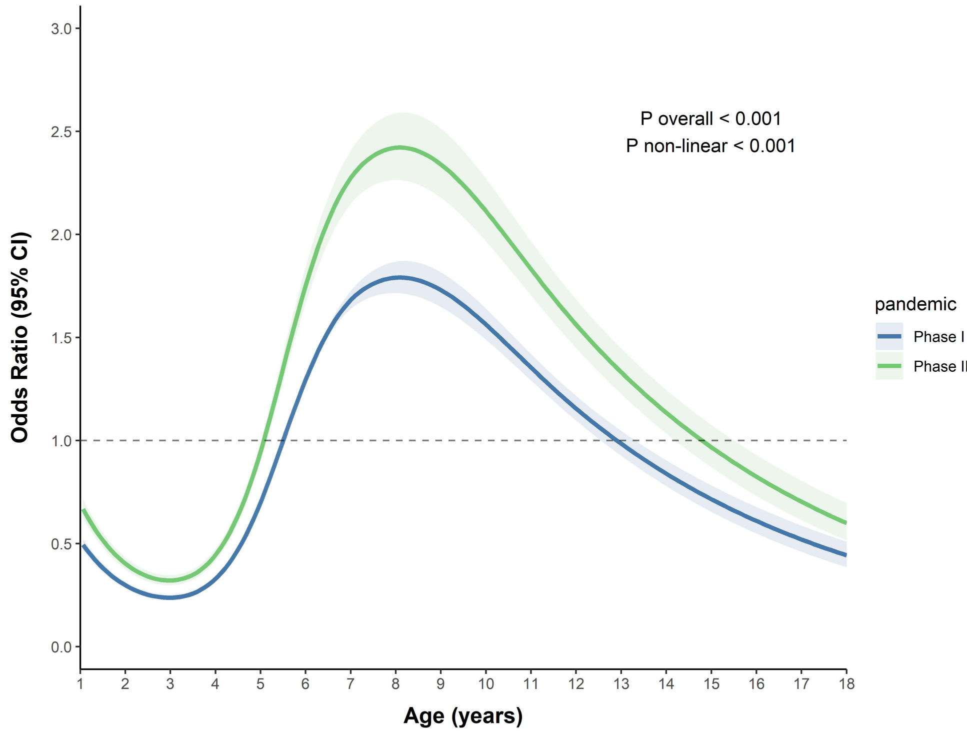


**Figure 3** Nonlinear association between age and risk of pertussis estimated by the restricted cubic spline regression model.

Moreover, it is crucial to acknowledge that during periods of low pertussis prevalence, such as in 2022 and 2023, physicians may primarily prescribe PCR testing for patients exhibiting classic symptoms, potentially leading to the oversight of asymptomatic cases. In the context of a notable rise in pertussis incidence and extensive transmission, physicians are inclined to utilize a more comprehensive array of diagnostic and laboratory tests to expedite the confirmation of pertussis infections. This approach potentially results in the identification of a larger number of pertussis cases, which could partially account for the elevated number of cases observed in 2024 in our study. Due to prolonged periods of low incidence, the decline in immunity may result in a gradual increase in the number of susceptible individuals.[13] Additionally, the absence of routine pertussis testing in adult healthcare facilities presents another potential factor: asymptomatic adults might have inadvertently transmitted the infection to children, thereby contributing to the current outbreak.

Our study observed notable differences in the results between Phase I and II, particularly in the proportion of hospitalized patients with suspected pertussis and the seasonality of cases. In Phase II, there was a higher number of hospitalized patients and a greater concentration of cases in spring. Regarding the increase in hospitalized patients in Phase II can be attributed to the resurgence of pertussis following the COVID-19 pandemic, during which many patients exhibited more severe symptoms, necessitating hospitalization. We attribute the seasonal increase in spring cases to the timing of our study, which coincided with a resurgence peak of pertussis, a period when cases and suspected cases typically surge. Additionally, heightened public awareness of pertussis during this time may have prompted more parents to seek testing for their children presenting with cough symptoms, leading to a sharp increase in testing volume.

Moreover, our study revealed notable fluctuations in pertussis detection rates throughout various stages of the COVID-19 pandemic. This variation can be ascribed to multiple factors. Primarily, the easing of stringent measures initially enacted to mitigate the spread of COVID-19 has increased the susceptibility to pertussis infections compared to the pandemic period, as the likelihood of pertussis transmission has risen. The non-linear association between age and pertussis risk identified in our analysis, along with the heightened odds ratios for pertussis infection observed post-pandemic relative to during the pandemic, further substantiates this finding. Secondly, the age range of children susceptible to pertussis expanded, as demonstrated by the non-linear regression analysis. Specifically, the susceptible age range increased from 5.7–12.4 years in Phase I to 5.1–14.6 years in Phase II (data not shown). This expansion

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suggests an increase in the potential population vulnerable to pertussis infection, thereby indicating a heightened disease burden within the entire pediatric population.

Our research indicates that after the ease of the COVID-19 measures, instances of pertussis emerged within the infant population in both outpatients and inpatients, particularly, in very young age groups (0–3 months, and 3–6 months), a phenomenon not observed during the pandemic period. One potential explanation is that the incidence of pertussis has prompted healthcare professionals to increase the frequency of pertussis testing to ensure that no suspected cases are overlooked. Furthermore, it is hypothesized that the COVID-19 pandemic has contributed to the issue of immunity debt. Immunity debt, or immunity gap, refers to the reduced herd immunity during the pandemic compared to before, caused by decreased exposure to microorganisms and lower vaccine uptake.[21] Another important factor is that China currently lacks a pertussis vaccine specifically recommended for pregnant women. Vaccinating pregnant women during the third trimester is crucial to provide passive immunity to newborns, protecting them from pertussis in early infancy.[22] As of now, acellular pertussis-containing vaccines for pregnant women in mainland China have not been incorporated into standard healthcare protocols.[23] Our results highlighted the necessary to vaccinate very young children. On December 25, 2024, the National Bureau of Disease Control and Prevention in China announced a revision to the national immunization program regarding the pertussis vaccine, marking a positive development. The previous schedule prescribes the administration of one dose of the DPT vaccine at the ages of 3 months, 4 months, 5 months, and 18 months for young children. From January 1, 2025, this schedule has been revised as the administration of a dose of the pertussis vaccine at 2 months, 4 months, 6 months and 18 months, and is implemented nationwide in China.

Our study also highlighted the relatively high detection rate of pertussis infection was observed in children older than 6 years regardless of the pandemic phases, seasons and patient types. The non-linear regression analysis showed that the age of highest risk of pertussis infection was 8.0 years in both pandemic phases. This finding may be attributed to the waning immunity from childhood pertussis vaccinations, as the protective effect of the vaccine diminishes over time, particularly in children who may not have received timely booster doses, rendering them more susceptible to infection.[13] Additionally, older children are more likely to be exposed to pertussis due to increased social interactions in school or community settings, where the risk of transmission is higher. Enhancing immunization efforts with pertussis-containing vaccines among pre-school children has been demonstrated to be an effective strategy for reducing pertussis morbidity across numerous countries. Our finding supported for the action of vaccinating children older than six years. In the previous national immunization program, children at age of six years would get a single dose of the adsorbed diphtheria-tetanus combined vaccine, has now been scheduled to receive an additional dose of the pertussis vaccine since 1 January 2025. The revised immunization program for pertussis vaccines in China aligns with international trends, as numerous other countries have implemented comparable strategies to address shifts in the pertussis epidemic. This initiative is expected to more effectively protect children's health.

## Conclusion

This study highlights the resurgence of pertussis among children in Eastern China, emphasizing significant epidemiological shifts and expanded age susceptibility after the COVID-19 pandemic, underscoring the urgent need for enhanced vaccination strategies and public health interventions. We suggest strengthening immunization coverage, enhancing public awareness, and implementing targeted surveillance to mitigate the observed trends and protect vulnerable groups.

## Strengths and Limitations

### Strengths

Our research had a number of strengths. First, the study utilized a large-scale sample of 92,300 children, providing sufficient statistical power to draw a solid conclusion. Second, this study utilized data from pertussis PCR test results, which offer higher diagnostic power compared to traditional bacterial cultures. Thirdly, we used restricted cubic spline regression models to evaluate the nonlinear relationship between age and the risk of pertussis infection.

## Limitations

Our research also had several limitations merit consideration. The present study was based in a single center, ie, Children's Hospital, Zhejiang University School of Medicine, in the East China. This is a tertiary hospital affiliated with a university and a national children's regional medical center. Despite the substantial sample size and its regional representativeness for children, it does not adequately reflect the overall pertussis infection status among children across China. Secondly, during periods of low pertussis prevalence, pertussis testing is predominantly prescribed by specialized clinics, such as those in infectious diseases and respiratory medicine, to confirm potential cases of pertussis infection. Conversely, during pertussis pandemics, a broader range of departments are likely to prescribe testing for children exhibiting pertinent symptoms, aiming to screen, confirm, or rule out pertussis infection. This shift in clinical practice may introduce bias. Thirdly, as our data were derived from a hospital laboratory testing system, representing real-world evidence, we did not have access to information on environmental factors such as air quality or regional climatic conditions. Additionally, data on underlying diseases were not routinely collected as part of the laboratory testing process, which restricted our ability to adjust for these potential confounders in our statistical models.

## Recommendations

Given the limitations of our study, we recommend that future research incorporates multi-center data to address the potential bias arising from relying on a single tertiary children's hospital dataset, ensuring broader representativeness of pertussis trends across diverse regions in China. Additionally, considering the possible influence of varying clinical practices on testing and diagnosis, standardized diagnostic criteria and testing protocols should be implemented in subsequent studies to minimize variability. Thirdly, there is the need for future research to incorporate broader data sources to account for more variables such as environmental factors and comorbidities. Last but not the least, longitudinal studies with detailed vaccination history data are encouraged to better understand the impact of waning immunity and missed booster doses on pertussis detection rates in different age groups.

## Data Sharing Statement

The data that support the findings of this study are available from the corresponding author, Dr Guannan Bai (Email: guannanbai@zju.edu.cn), upon reasonable request.

## Ethics Statement

The study was approved by the medical ethics committee of Children's Hospital, Zhejiang University School of Medicine (No. 2024-IRB-0117-P-01).

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## 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. Linli Wang and Meiying Gao contributed equally to this work and shared the first authorship. Yang Yang and Guannan Bai contributed equally to this work and shared the last authorship.

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## Disclosure

The authors declare no conflict of interest.

## References

1. Nieves DJ, Heininger U. Bordetella pertussis. *Microbiol Spectr*. 2016;4(3). doi:10.1128/microbiolspec.EI10-0008-2015
2. Mattoo S, Cherry JD. Molecular pathogenesis, epidemiology, and clinical manifestations of respiratory infections due to Bordetella pertussis and other Bordetella subspecies. *Clin Microbiol Rev*. 2005;18(2):326–382. doi:10.1128/CMR.18.2.326-382.2005
3. Tan T, Dalby T, Forsyth K, et al. Pertussis across the globe: recent epidemiologic trends from 2000 to 2013. *Pediatr Infect Dis J*. 2015;34(9):e222–32. doi:10.1097/INF.0000000000000795
4. Crowcroft N, Miller E. Pertussis epidemiology. *Pertussis*. 2019;66–86.
5. Cherry JD, Paddock CD. Pathogenesis and histopathology of pertussis: implications for immunization. *Expert Rev Vaccines*. 2014;13(9):1115–1123. doi:10.1586/14760584.2014.935766
6. Fullen AR, Yount KS, Dubey P, Deora R. Whoop! There it is: the surprising resurgence of pertussis. *PLoS Pathog*. 2020;16(7):e1008625. doi:10.1371/journal.ppat.1008625
7. Lin L-N, Zhou J-S, Hua C-Z, Bai G-N, Mi Y-M, Zhou -M-M. Epidemiological and clinical characteristics of pertussis in children and their close contacts in households: a cross-sectional survey in Zhejiang Province, China. *Front Pediatr*. 2022;10:976796. doi:10.3389/fped.2022.976796
8. Decker MD, Edwards KM. Pertussis (whooping cough). *J Infect Dis*. 2021;224(Supplement_4):S310–S20. doi:10.1093/infdis/jiaa469
9. Overview of national statutory infectious disease epidemic in 2019 [Internet]. Beijing (China): National Disease Control and Prevention Administration [updated 2024 April 20; cited 2024 October 13]. Available from: https://www.ndcpa.gov.cn/jbkzzx/c100016/common/content/content_1782571426407886848.html. Accessed August 19, 2025.
10. Overview of national statutory infectious disease epidemic in august 2024 [Internet]. Beijing (China): National Disease Control and Prevention Administration [updated 2024 September 13; cited 2024 October 13]. Available from: https://www.ndcpa.gov.cn/jbkzzx/c100016/common/content/content_1834433420274282496.html. Accessed August 19, 2025.
11. Overview of national statutory infectious disease epidemic in 2023[Internet]. Beijing (China): National Disease Control and Prevention Administration [updated 2024 September 18; cited 2024 October 13]. Available from: https://www.ndcpa.gov.cn/jbkzzx/c100016/common/content/content_1836299733133275136.html. Accessed August 19, 2025.
12. Huang H, Zhu T, Gao C, et al. Epidemiological features of pertussis resurgence based on community populations with high vaccination coverage in China. *Epidemiol Infect*. 2015;143(9):1950–1956. doi:10.1017/S095026881400260X
13. He H, Zhu Y, Jin M, et al. The decline in immunity and circulation of pertussis among Chinese population during the COVID-19 pandemic: a cross-sectional sero-epidemiological study. *Vaccine*. 2022;40(48):6956–6962. doi:10.1016/j.vaccine.2022.10.020
14. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA*. 2013;310(20):2191–2194. doi:10.1001/jama.2013.281053
15. Anderer S. Whooping cough cases rise in Latin America and the US in 2024. *JAMA*. 2024;332(11):865.
16. Khalil A, Samara A, Campbell H, Ladhani SN, Amirthalingam G. Recent increase in infant pertussis cases in Europe and the critical importance of antenatal immunizations: we must do better…now. *Int J Infect Dis*. 2024;146:107148. doi:10.1016/j.ijid.2024.107148
17. Hua C-Z, He H-Q, Shu Q. Resurgence of pertussis: reasons and coping strategies. *World J Pediatr*. 2024;20(7):639–642. doi:10.1007/s12519-024-00821-2
18. Bouchez V, Guiso N. Bordetella pertussis, B. parapertussis, vaccines and cycles of whooping cough. *Pathog Dis*. 2015;73(7). doi:10.1093/femspd/ftv055
19. Zhang J, Deng J, Yang Y. Pertussis vaccination in Chinese children with increasing reported pertussis cases. *Lancet Infect Dis*. 2022;22(1):21–22. doi:10.1016/S1473-3099(21)00752-0
20. Zhang Z, Pan J, Chen M, Zhang T, Li J, Lu L. Seroepidemiology of pertussis in China: a population-based, cross-sectional study. *Vaccine*. 2021;39(12):1687–1692. doi:10.1016/j.vaccine.2021.02.032
21. Han P, Shen K. Covid lockdown and repaying the immunity debt in children. *Glob Pediatr*. 2024;9:100195. doi:10.1016/j.gpeds.2024.100195
22. Ren J, Huang Z, Tian J, et al. Evaluation of pre-school pertussis booster vaccination in Shanghai, China: a cost-effectiveness analysis. *Vaccine*. 2024;42(21):126162. doi:10.1016/j.vaccine.2024.126162
23. Jiang F, Ye X, Wang Y, et al. Factors associated with pregnant women's willingness to receive maternal pertussis vaccination in Guizhou Province, China: an exploratory cross-sectional study. *Hum Vaccin Immunother*. 2024;20(1):2331870. doi:10.1080/21645515.2024.2331870