EVALUATION OF TREATMENT OUTCOMES FOR PEDIATRIC PATIENTS WITH PERTUSSIS AT THE VIETNAM NATIONAL CHILDREN'S HOSPITAL, 2019-2020

Hoang Dinh Canh [1], Truong Van Tu [2] Cao Ba Loi[1*]
National Institute of Malariology Parasitology and Entomology
[2] *Navy Medical Department*

Abstract

Pertussis is a respiratory tract infection caused by Bordetella pertussis, particularly affecting children and often leading to prolonged and distressing coughing episodes. The aim of the study was to determine the cure rate, complications, and mortality in children with pertussis at the National Children's Hospital. A cross-sectional descriptive study was conducted on 382 children under 16 years old diagnosed with pertussis at the National Children's Hospital from January 1, 2019 to December 31, 2020. 95.5% (365/382) of the children were prescribed macrolide antibiotics. 12.3% (47/382) of the children were hospitalized in the Intensive Care Unit with an average stay of 10 days (ranging from 1 to 60 days). 44.5% (170/382) required oxygen therapy; 9.2% (35/382) needed mechanical ventilation; 4.5% (17/382) received intravenous immunoglobulin (IVIG); 0.8% (3/382) required extracorporeal membrane oxygenation (ECMO); and 0.5% (2/382) underwent blood filtration. After an average 25.8 ± 10.5 days, Real-time PCR results confirmed negative. The cure rate was 92.9% with an average hospital stay of 12.95 ± 10.47 days. The children with severe pertussis had a nearly twice as long average hospital stay (15 days) as those with mild and moderate pertussis (8 days). The mortality rate was 1.6%. Macrolide antibiotics remained highly effective in the treatment of pertussis with the cure rate of 92.9%.

Key words: Pediatric patient, pertussis, treament, cured.

1. Introduction

Bordetella pertussis (B. pertussis), causing whooping cough (pertussis) which is an acute respiratory infectious disease, can cause epidemics and is common in young children. The epidemiological situation of pertussis worldwide remains a major concern for global health organizations. Despite being controlled through national immunization programs, there are still areas and communities that have not achieved full immunization coverage, leading to the emergence of new outbreaks and infections. There are about 30 million cases of pertussis worldwide each year, including 160,700 deaths which are mainly children under 5 years old [1]. In spite of the presence of vaccines for the disease, the incidence in many countries is increasing due to many different related factors. WHO considers pertussis a re-emerging disease. In Vietnam, pertussis remains a major public health problem. Although national immunization programs have achieved some success, additional efforts are needed to ensure

[*] *E-mail address:* caoloi28111964@gmail.com
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adequate immunization coverage and provide accurate information on symptoms, prevention, and treatment for the community. Pertussis incidence has been on the rise since 2015 [2,3]. Clinical symptoms in children with pertussis vary widely, and complications are rather serious, including severe pneumonia, respiratory failure, pulmonary hypertension, and possible death. Antibiotics are often used to reduce the severity of the disease, especially at the onset. However, management of pertussis is not limited to treatment but also involves regular vaccination, community education on preventive measures, and improved medical diagnosis. This poses a significant challenge in controlling and preventing the spread of the disease. Given the urgency of identifying factors associated with pertussis in children, we conducted the study "*Evaluation of treatment outcomes for pediatric patients with pertussis at the National Children's Hospital from January 2019 to December 2020*" with the aim of determining the cure rate, severe complications and mortality in the children with pertussis treated at the National Children's Hospital.

2. Subjects and methods

2.1 Subject, location, and duration

- Subjects: Children under 16 years old diagnosed with pertussis.

- Location: At the National Children's Hospital.

- Duration: From January 1, 2019 to December 31, 2020

2.2 Methods

The study was designed using cross-sectional descriptive research method.

The sample size was calculated as follows.

$n = Z^2_{1-\alpha/2} \frac{1-p}{p.\omega^2}$. In which n is the minimum sample size; p is the cure rate p = 0.719;, Z is the reliability coefficient, with α = 0.05 then $Z_{1-\alpha/2}$ = 1.96, ω allowable relative error, choose ω = 0.06. With the selected values, the minimum sample size was 213. In this study we selected 382 pediatric patients.

Inclusion criteria: Select all the children under 16 years old who met diagnostic criteria for pertussis according to the guidelines by the National Children's Hospital.

Techniques used in the study included clinical examination and paraclinical testing techniques served for treatment.

2.3 Data analysis

Data were entered and analyzed using Stata and SPSS 22.0 software.

2.4 Research ethics

The study was conducted under the approval and consensus by the Board of Directors and the Ethics Council of the National Children's Hospital. The participants in the study were well informed of the content and purpose of the study. They voluntarily participated in the study and provided accurate and objective information. Their personal information was kept confidential.

3. Results

3.1. Treatment

3.1.1. Treatment with macrolide antibiotics

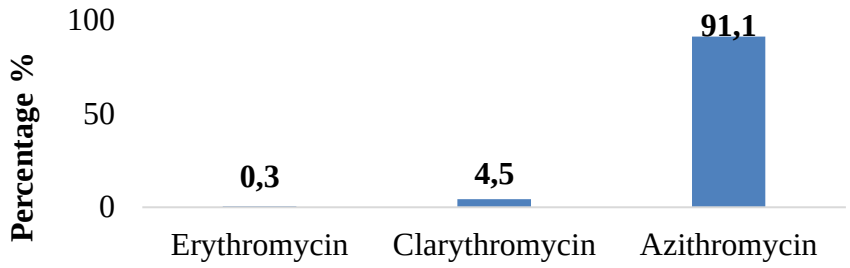

Figure 1. Proportion of macrolide antibiotic use (n = 382)

95.5% (365/382) of the children were prescribed macrolide antibiotics at the hospital, of which 91.1% (348/382) were given azithromycin, 4.5% (17/382) were given clarithromycin, and only 0.3% (1/382) were given erythromycin. The average duration of treatment: $\bar{x} \pm SD = 7.17 \pm 2.63$ (days).

3.1.2. Treatment with other antibiotics (Non-Macrolide)

73.3% (280/382) of the children used non-macrolide antibiotics.

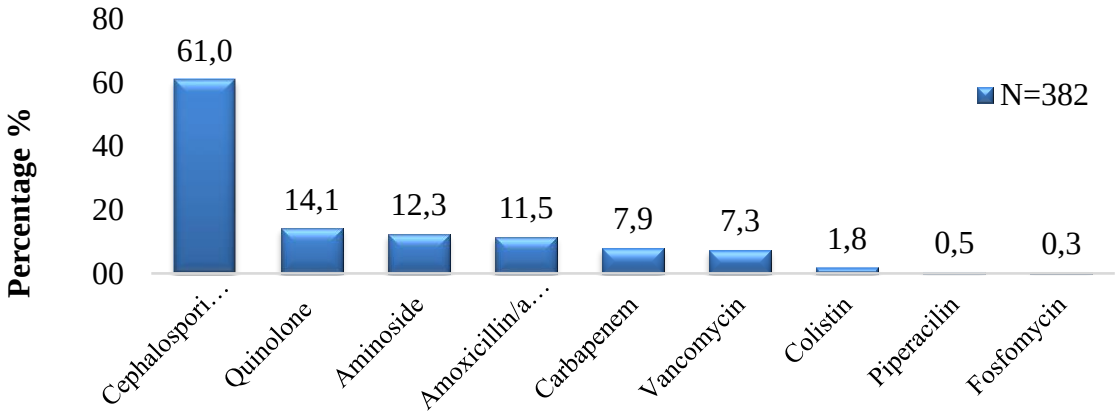

Figure 2. Proportion of non-macrolide antibiotic use (n = 382)

The most commonly used non-macrolide antibiotics were third generation cephalosporins, including ceftriaxone, ceftazidime, cefoperazole, cefotaxime, ...

3.1.3. Rate of antibiotic use according to the severity of pertussis

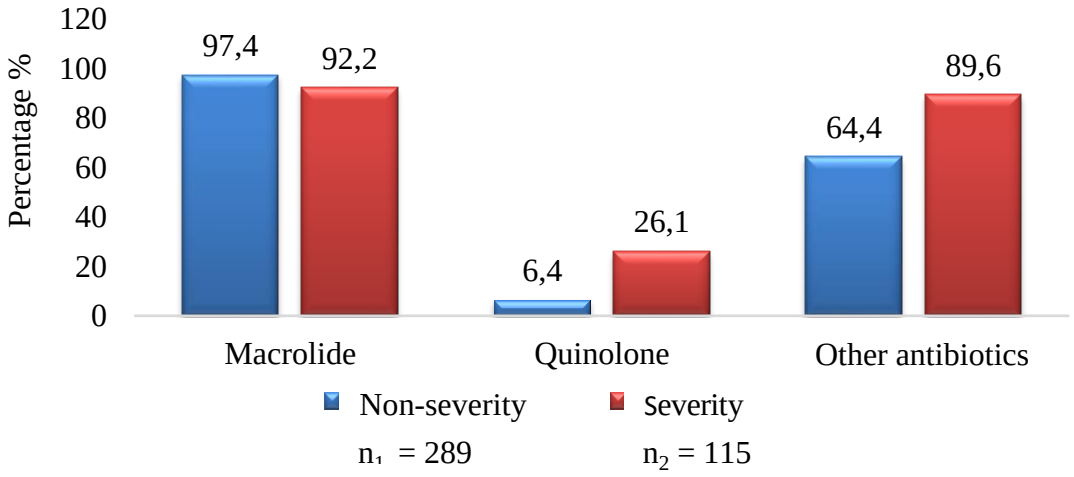

Figure 3. Proportion of macrolide, quinolone and other antibiotic use according to the severity of pertussis

The number of children with severe pertussis using macrolides was less than those using other antibiotics (92.2% vs. 97.4%), however the proportion of severe patients using quinolone and other antibiotics was more than those without severity; the difference was statistically significant ($p < 0.05$).

3.1.4. Other supportive treatment drugs

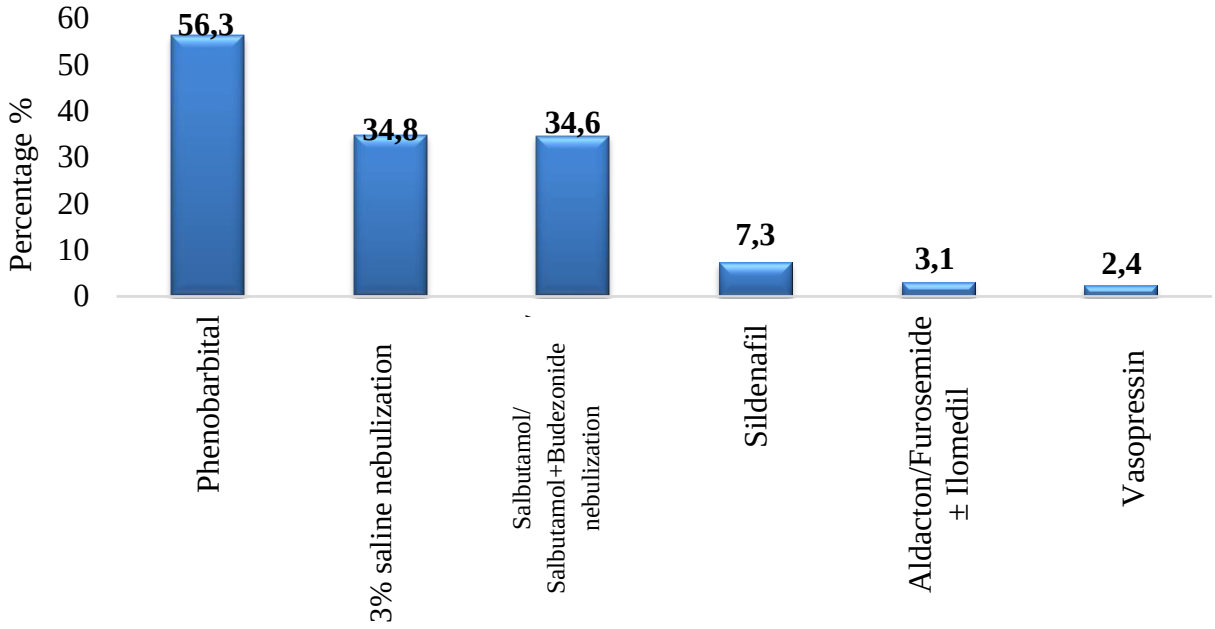

Figure 4: Other supportive treatment drugs (n = 382)

Some supportive drugs for treatment of pertussis in young children included phenobarbitals (56.3%) which help to suppress coughs by neurological mechanisms, nebulization with saline 0.9%, or hypertonic saline 3% (34.8%), aerosolized bronchodilators (salbutamol) which can be combined with anti-inflammatory drugs (budesonide) (34.6%), supportive drugs to treat pulmonary arterial hypertension such as sildenafil (7.3%), lasix or aldactone (3.1%), and some cases of circulatory resuscitation using vasopressors (2.4%).

3.1.5. Resuscitation therapies

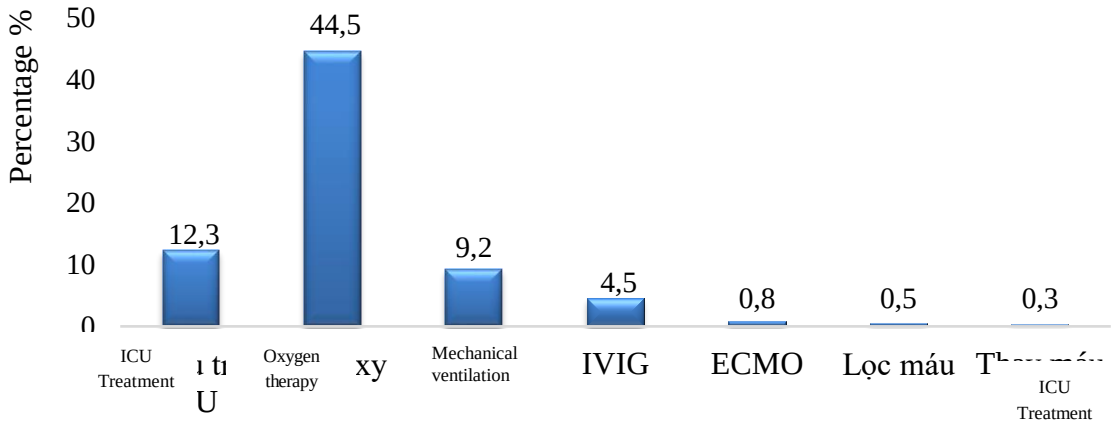

Figure 5. Resuscitation therapies for severe pertussis (n = 382)

12.3% (47/382) of the children with pertussis were hospitalized in the Intensive Care Unit with the average stay of 10 days (ranging from 1 to 60 days).

44.5% (170/382) of the children required oxygen, of which 15.4% (59/382) required intermittent oxygen therapy during cough attacks, and 29.1% (111/382) of the children with respiratory failure required continuous oxygen therapy. 9.2% (35/382) needed mechanical ventilation; 4.5% (17/382) required IVIG, 0.8% (3/382) required ECMO, 0.5% (2/382) required blood filtration, and 0.3% (1/382) required exchange transfusion.

3.2. Treatment outcomes

3.2.1. Real-time PCR results after treatment

Among 65 children undergoing second time PCR for pertussis, 30 (46.2%) children were confirmed positive, and 35 (53.8%) children were confirmed negative for pertussis after a period of treatment. After an average 10.4 ± 7.6 days after hospital admission, second time PCR was conducted.

Table 1. Real-time PCR results after a period of pertussis treatment

	Second time Real-time PCR (+)(n_1 = 30)	Second time Real-time PCR (-)(n_2 = 35)	P
Average hospital stay until positive real-time PCR confirmation	18.4 ± 8.9	25.8 ± 10.5	0.007
Average treatment duration from admission to negative PCR confirmation	8.7 ± 7.5	10.4 ± 8.5	0.45

After an average 25.8 ± 10.5 days, Real-time PCR of pertussis changed from negative to positive; the average treatment duration until negative confirmation by second time PCR was 10.4 ± 8.5 days.

3.2.2. Treatment duration

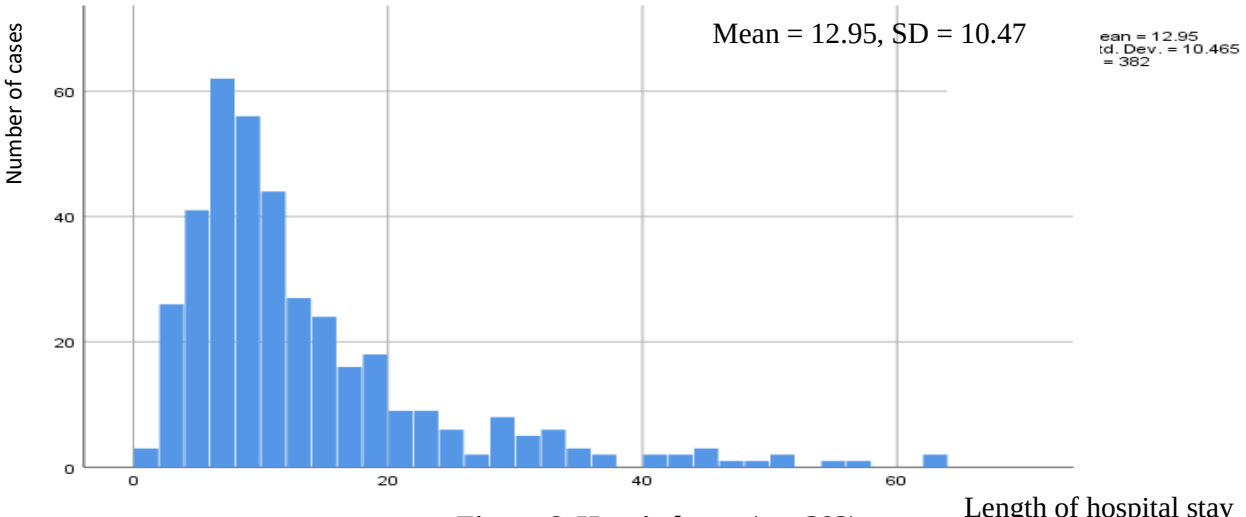

Figure 6. Hospital stay (n = 382)

The average length of hospital stay was $\bar{x} \pm SD = 13.0 \pm 10.47$ (days) with the median of 10 days (ranging from 1 day to 62 days); only 8.6% (33/382) of the children stayed in hospital within 1 week.

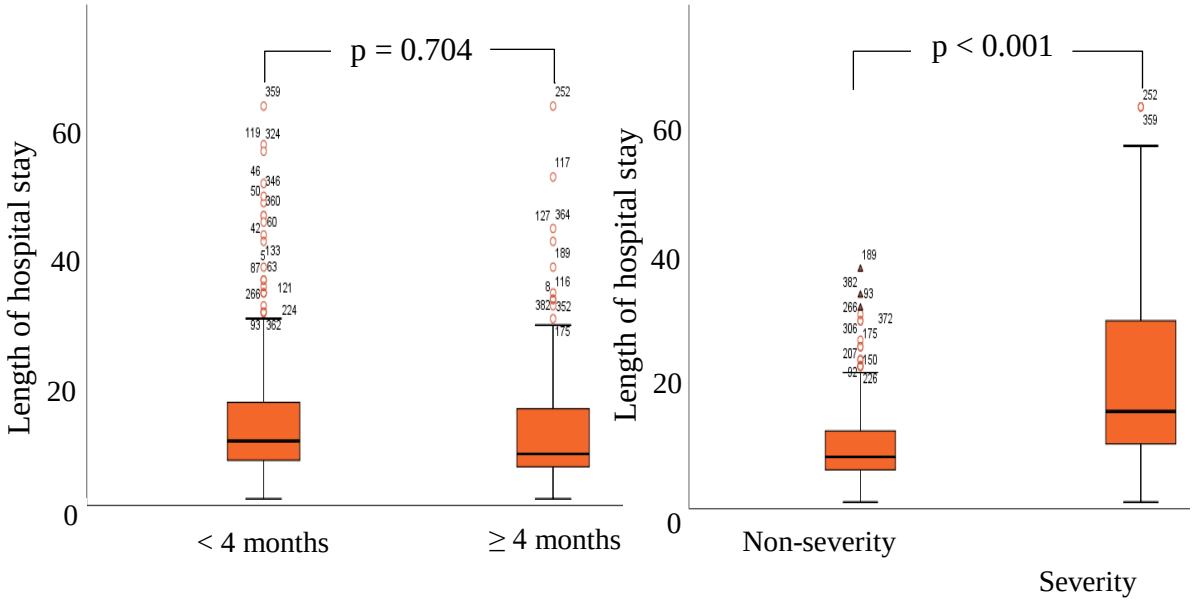

Figure 7. Hospital stay by age and severity (n = 382)

There was no difference in the length of hospital stay between age groups ($p > 0.05$). The median hospital stay for severe pertussis was 15 days (ranging from 1 day to 37 days), nearly twice as long as the median hospital stay for non-severe pertussis, which was 8 days (ranging from 1 day to 62 days) ($p < 0.01$).

3.2.3. Patient discharge status

In this study, we divided the results into 4 levels: 1. Cured, 2. Required readmitted to hospital, 3. Hospital transfer, 4. Death or very high risk of death, which was shown in Figure 8.

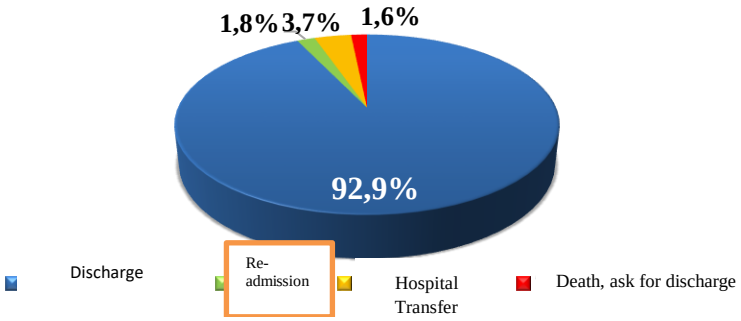

Figure 8. *Patient discharge status* (n = 382)

The treatment outcomes for pertussis were good in general with the cure rate of 92.9% (355/382). A few children (1.8%) required hospital readmission due to again

cough attacks. Only 1.6% (6/382) of the children died from pertussis complications.

4. Discussion

The average length of hospital stay for the pediatric patients in our study was 13.0 ± 10.47 days with the median of 10 days (ranging from 1 day to 62 days). It is higher than that in the report by Tran Minh Dien (2015) which was 6 days (ranging from 1 day to 50 days) [2]. The study on pertussis children aged under 3 months old in California by Nieves (2010) also found that the average length of hospital stay was 11 days [6]. However, our finding is similar to the result by Castagnini which studied infants with pertussis; according to Castagnini the average length of hospital stay was 14.5 days with the median of 10 days [5]. In this study, the median length of hospital stay in children under 4 months old was 10 days (IQR 1-62 days), and it was 8 days (IQR 1-62 days) in children ≥ 4 months old; the difference was not statistically significant ($p > 0.05$). However, according to Cortese's report, the median length of hospital stay was different by age groups such as: newborns, 6 days, 1-2 months old: 4 days, 3-6 months old: 3 days, 7-11 months old: 2 days [7]. This difference may be due to the fact that Cortese's study divided subjects into many age groups, especially the group of newborns had a longer treatment duration than other age groups.

In this study, the length of hospital stay was different between the severe and non-severe groups, specifically 15 days and 8 days respectively, ($p < 0.05$).

We found that most (92.9%) of the children with pertussis recovered well and were discharged from the hospital without sequelae, while 1.6% (6/382) of the patients died. This cure rate is higher than that (79.6%) by Do Thien Hai (2021) [8] and Vieira's report on pertussis in northern Portugal with the mortality rate of 0.3% but lower than that in our study conducted in the period 2012 - 2014, which reported the mortality rate of 2.8% [9]. According to the World Health Organization, the mortality of pertussis in children is about 4% [10]. This rate is lower than Nieto Gueva's report on pertussis in Panama from 2001 to 2008, which showed a mortality rate of 8.3%, of which more than half were children under 1 month old [11]. Another study by Surridge on a group of children with severe pertussis treated at a pediatric intensive care unit in New Zealand showed a mortality rate of 5.6% [12]. In particular, Nieves' study on pertussis in children under 3 months old in California, USA in 2010 found a mortality rate of more than 30% (10/32) [6]. This shows that although pertussis was widely vaccinated globally 40-50 years ago, the disease still occurs in many countries, including developed countries with high vaccination rates; and the disease is still a life-threatening danger, especially for young children. In addition, pertussis has a prolonged course, requiring follow-up after discharge and sometimes re-hospitalization.

5. Conclusion

95.5% of the children with pertussis were specifically treated with macrolide antibiotics, mainly azithromycin (91.1%). However, there has been a rise in antibiotic resistance so for severe cases that do not respond to treatment, other antibiotics such as Quinolone (14.1%), third generation cephalosporin (61.0%) must be used... The cure rate of pertussis in our study was 92.9% with the average length of hospital stay of 12.95 ± 10.47 days. The children with severe pertussis stayed in hospital (median 15 days) nearly twice as long as the group with non-severe pertussis (median 8 days). This showed that pertussis is still a dangerous disease that can cause death in young children with the mortality rate of 1.6%. Therefore, children are highly recommended to be fully vaccinated against pertussis.

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