

ORIGINAL ARTICLE

**PERTUSSIS RESURGENCE IN CHILDREN:
A CROSS-SECTIONAL, SINGLE CENTRE
STUDY IN NORTH-WEST MALAYSIA**

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Abstract

Introduction: Vaccine-preventable diseases such as pertussis are re-emerging in Malaysia during recent years. **Objective:** This research aims to study the local incidence of clinical pertussis among paediatric patients admitted to Hospital Tuanku Fauziah, Perlis over two-year period. **Method:** A cross-sectional study was designed in Department of Paediatrics, Hospital Tuanku Fauziah, Perlis from 1 January 2013 till 31 January 2015. Data were collected from medical and laboratory record of cases admitted for clinical pertussis. Analyses for descriptive data were done using frequency and percentage; Pearson chi-square or Fisher exact was used to test association. **Results:** 81 cases of clinical pertussis were included in the study. Out of this, there were a total of 28 confirmed cases of pertussis. There was a steady increment in the incidence of pertussis throughout the study period. Cyanosis emerged as the only clinical sign significantly associated with pertussis ($p = 0.011$). Majority of the confirmed pertussis cases were too young to be immunized ($n = 13, 46.4\%$). **Conclusion:** Reappraisal of local health system to strengthen herd immunity in the community is warranted to control disease spread.

Keywords: Pertussis, Immunization, Whooping Cough, Incidence, Respiratory Insufficiency

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Introduction

Pertussis is caused by *Bordetella pertussis*, a uniquely human pathogen. It is a gram-negative bacterium causing acute infection of the respiratory tract. It is primarily transmitted through aerosolised droplets of

secretions from respiratory tracts [1]. Apart from that, it can also be transmitted via direct contact with respiratory secretions of an infected person. Catarrhal stage of the disease occurring in the first two weeks of the disease may mimic other acute respiratory illness and is highly contagious.

Paroxysmal stage begins after two weeks of illness and can last up to four weeks, typically associated with coughing spells and inspiratory whoops.

Pertussis is a notifiable disease with significant relevance for public health planning. The United States still experiences pertussis epidemic cycles every 3 to 4 years [2]. Since 1948, whole cell pertussis vaccine (DTwP) has been used worldwide but was later switched to acellular pertussis (DTaP) in 1990s due to safety concerns [3].

In Malaysia, yearly incidence of pertussis causes substantial morbidity in paediatrics population. The disease is highly contagious and has a remarkable capacity to spread, thus demanding for a continual surveillance by public health personnel. Acellular pertussis vaccine was only introduced in Malaysia in the year 2008 and polymerase chain reaction (PCR) laboratory test was only made available in Institute of Medical Research (IMR), Malaysia beginning the year 2010. The recent rise of anti-vaccine movement in Malaysia has exposed the country to unnecessary threat of the emergence of old diseases, such as pertussis and measles. Ministry of Health in a press statement in 2016 has reported a 4-fold increment in the number of pertussis cases documented, from 222 cases in 2013 to 939 cases in 2015. Despite the growing local health measures to educate the public regarding the importance to comply to the vaccination program, there are still isolated groups who still failed to appreciate the concept of herd immunity. A local study conducted in Hulu Langat Selangor in 2016 found that the main reason for parents not vaccinating their children was due to the impression that “vaccinations are dangerous” [4]. Malaysian data on pertussis, particularly among children are scarce.

The research was designed to study the local incidence and demographic profile of paediatric patients admitted with clinical pertussis in Hospital Tuanku Fauziah, Perlis.

Methods

This study was conducted in Hospital Tuanku Fauziah, Perlis, a public hospital in the northern part of Malaysia. The hospital provides tertiary care level to an estimated population of 300,000 people. The hospital is equipped with two general paediatrics wards with the capacity to accommodate 60 beds and a 4-bedded paediatrics intensive care unit. Five general paediatricians are stationed in this hospital.

A cross-sectional study was conducted in the Department of Paediatrics from 1st January 2013 to 31st January 2015. Hospital medical records and laboratory data were obtained from the record unit and relevant data were extracted into a separate data collection sheet.

Selection and Description of Participants

We included all patients under the age of 12 years old who were admitted with clinical suspicion of pertussis. Clinical sign and symptoms commonly associated with pertussis in children are different according to different age at presentation. Hence, for children aged from 0 to 3 months old, clinical pertussis is suspected if they presented with cough of any duration which does not improve and may be seen as paroxysmal, coryza which does not become purulent, low-grade fever and association with with apnoea, seizures, cyanosis or emesis. For those children aged 4 months and above, clinical pertussis is suspected if they presented with paroxysmal non-productive cough of at least 7 days duration and is associated with coryza which does not

become purulent, low-grade fever, apnoea, post-tussive emesis, subconjunctival hemorrhage, cyanosis or whoop. Exclusion criteria include children who were immunocompromised or cases with incomplete relevant clinical data in the medical record. Relevant clinical data include complete documentation of presenting sign and symptoms.

Nasopharyngeal swab (NPS) samples were taken from all patients admitted for clinical pertussis. The sample was sent to Institute of Medical Research (IMR) for polymerase chain reaction (PCR) testing of *Bordetella pertussis*. Cases with laboratory-confirmed pertussis were labelled as NPS-positive, as opposed to NPS-negative, indicating other acute respiratory illnesses. Nonetheless, all patients were treated with macrolide group of antibiotics following standard pertussis treatment.

This study was registered in the National Medical Research Register of Malaysia (ID: NMRR-15-99-24307).

Technical Information

NPS swab sample was taken in all cases. A Dacron swab on a soft flexible wire was passed into the nostril and along the floor of the nasal cavity into the posterior nasopharynx. The swab was then rotated to complete a cycle and was gently withdrawn. It was then placed in a transport medium, the Stuart's media and sent to the hospital

laboratory immediately. The specimens were then transported at 4°C reaching the centralised IMR lab within 3 days of sampling. All of the cases were notified to the local health department using Notice Form (Health 1 Rev. 2001) within 24 hours of NPS sampling.

Statistics

The data were analysed with IBM SPSS Statistics version 20.0.0. Categorical variables were presented as frequencies with percentages and were compared using chi-square test. Continuous variables that were normally distributed are presented as mean and standard deviation and compared using *t*-test. For non-normally distributed data, median and interquartile range was presented. Statistical significance was taken at $p < 0.05$.

Results

There were a total of 81 cases of clinical pertussis admitted to Department of Paediatrics, Hospital Tuanku Fauziah, Perlis from 1 January 2013 until 31 January 2015. Out of this, a confirmed 28 cases of pertussis were detected.

Socio-demographic data between laboratory-confirmed NPS-positive and NPS-negative diagnoses among clinical pertussis cases were compared in Table 1.

Table 1. Baseline sociodemographic characteristics among cases of admitted for clinical pertussis

Characteristics	NPS negative Frequency, <i>n</i> = 53 <i>n</i> (%)	NPS positive Frequency, <i>n</i> = 28 <i>n</i> (%)	<i>p</i>-value
Gender			0.254 ^a
Male	37 (69.8)	16 (57.1)	
Female	16 (30.2)	12 (42.9)	
Age†			0.973 ^b
Newborn (≤ 28 days)	7 (13.2)	4 (14.3)	
29 days - ≤ 3 months	29 (54.7)	15 (53.6)	
3 - 5 months	9 (17.0)	5 (17.9)	
6 - 11 months	4 (7.5)	3 (10.7)	
1 - 5 years	4 (7.5)	1 (3.6)	
Ethnicity			1.000 ^b
Malay	52 (98.1)	27 (96.4)	
Non-malay	1 (1.9)	1 (3.6)	
Contact with ill people			0.288 ^a
Yes	13 (24.5)	10 (35.7)	
No	40 (75.5)	18 (64.3)	
Length of hospitalization (days)* †	5.0 (4.00)	5.5 (7.00)	0.346 ^c

*presented as median and interquartile range

† skew to the right

^aPearson chi-square test of independence

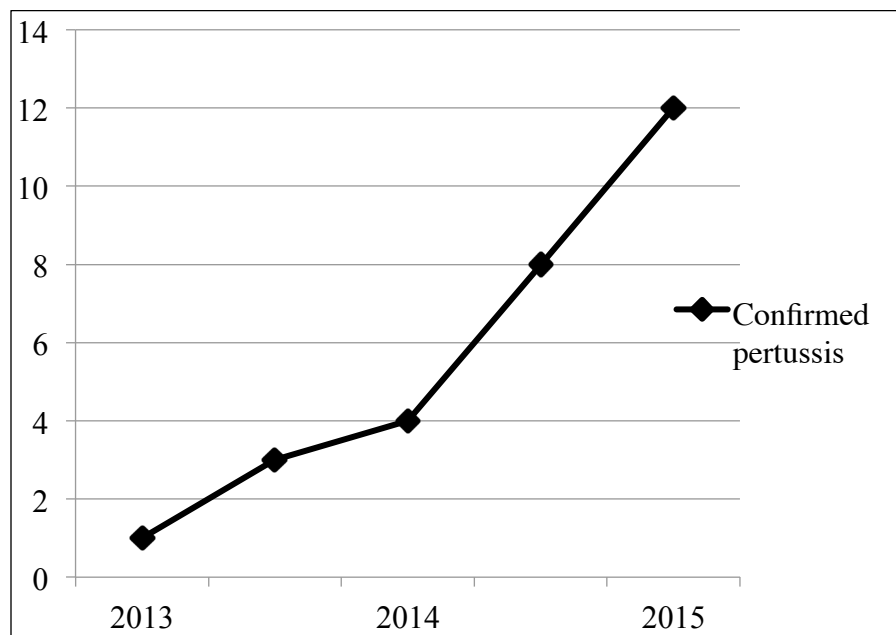
^bFisher exact test

^cMann-Whitney U test

Out of the total 81 admissions for clinical pertussis, majority were boys (*n* = 53, 65.4%) and most of the cases admitted were Malays (*n* = 79, 97.5%). There was a steady

increment in the number of laboratory confirmed pertussis cases as seen in Figure 1.

Figure 1. Trend of NPS-positive cases between January 2013 – January 2015 in Hospital Tuanku Fauziah, Perlis



The median age of confirmed pertussis cases (NPS-positive) was 2.0 months old (IQR = 2.80). The median duration of hospitalization among confirmed pertussis cases was 5.5 days (IQR = 7.00). A large majority of the patients did not report history of sick contact prior to the onset of illness ($n = 58, 71.6\%$). Common presenting signs and symptoms among the confirmed pertussis cases include apnoea ($n = 25, 89.3\%$), coryza ($n = 16, 57.1\%$), pulmonary

signs as evident by the presence of crepitations on auscultation ($n = 16, 57.1\%$), respiratory distress ($n = 16, 57.1\%$) and fever ($n = 14, 50.0\%$). Majority of the confirmed pertussis cases had lymphocytosis ($n = 19, 67.9\%$) as compared to thrombocytosis. Cyanosis was the only clinical sign that was significantly associated with pertussis, $\chi^2 (df = 1, n = 28) = 6.39, p = 0.011$, as observed in Table 2.

Table 2. Association between clinical characteristics and laboratory-confirmed pertussis cases

Clinical characteristics	NPS negative n (%)	NPS positive n (%)	χ^2	df	p-value ^a
Fever	33 (62.3)	14 (50.0)	1.13	1	0.287
Coryza	32 (60.4)	16 (57.1)	0.08	1	0.778
Paroxysmal cough	16 (30.2)	12 (42.9)	1.30	1	0.254
Cyanosis	9 (17.0)	12 (42.9)	6.39	1	0.011*
Pulmonary sign	26 (49.1)	12 (42.9)	0.28	1	0.595
Vomit	12 (22.6)	12 (42.9)	3.59	1	0.058
Respiratory distress	34 (64.2)	16 (57.1)	0.38	1	0.537

^aPearson chi-square test of independence

*Statistically significant

All of the confirmed pertussis cases have not completed immunizations. Majority were too young to be immunized ($n = 13$, 46.4%), the rest did not complete immunization ($n = 11$, 39.3%) and were unimmunized at all ($n = 4$, 14.3%).

Majority of the cases either completed 14 days of treatment course with erythromycin ethylsuccinate ($n = 73$, 90.1%) or seven days treatment course with clarithromycin ($n = 4$, 4.9%). The rest was given Bactrim due to history of allergy to macrolide.

Discussion

Perlis is the smallest state in Malaysia with an area of 317 square miles with an estimated population of 300,000. It is situated in the west Peninsula and bordered by Thailand up north. There were a total of 28 confirmed cases of pertussis recorded within 25-month study period between 1 January 2013 and 31 January 2015.

There was a steady increment in the number of confirmed pertussis cases admitted to Department of Paediatrics, Hospital Tuanku Fauziah, Perlis, Malaysia. In the last two decades, Malaysia has been witnessing a rise in the number of reported cases of pertussis. This observation draws attention for public health control measures as increasing hospital burden leads to a consequent economic impact on consumed health resources [5]. The rise in pertussis cases may also be closely related to immunisation coverage as a vast majority of the patients did not complete vaccination. This is supported by a study conducted by Lim et al. in 2016 which found that Malaysia immunisation coverage was only at 86.4%, a considerably low number than the target set at 95% [6]. Apart from the popular postulation of waning herd immunity within the community [7], pertussis resurgence may

also be contributed by an increased in awareness and vigilance among primary physicians and better access to the use of laboratory diagnostics, especially with the introduction of PCR testing in Malaysia. The growing misconception about vaccination which merely stemmed out from isolated fictitious ideas among the public has led to dissemination of propaganda spread across social media platform, hence leading to rise of anti-vaccine movement.

In the study, the median age of presentation was 2 months old (IQR=2.80). This strongly correlates to the known clinical epidemiology of pertussis, indicating that pertussis is, but not exclusively a disease of infancy and childhood [1, 8]. Chuah have found that infants aged less than 3 months old were more susceptible to critical pertussis than those in older age group [9].

The median duration of hospitalization in the study was 5.5 days (IQR=7.00) indicating early treatment response to timely management. Our finding is comparable to an intervention study done implementing the Family Cocooning Program, an initiation to immunise whole family members to protect the newborns. They found that the mean of hospital stay was reduced to 6.7 days from 8.9 days in successful Family Cocooning Program [10]. Treatment in the early course of the disease may lessen the symptoms and reduce the risk of severe and complicated disease, especially in infants [2]. Majority of the confirmed pertussis cases were found to be too young to be immunised, hence warranting the need to strengthen herd immunity. Majority of the confirmed pertussis cases denied history of contact with ill person. This typically corresponds to the nature of the disease spread. Its airborne mode of transmission is not always easy to substantiate, thus the history of contact with

ill person may not be generally demonstrable.

The study found that the presence of fever, coryza, apnea, lungs crepitations and respiratory distress were common among pertussis patients but were not significantly associated with pertussis. Presence of cyanosis on the other hand, was found to be the key feature in pertussis. Cyanosis results from severe hypoxaemia occurring during episodic bouts of violent cough [11, 12]. Lymphocytosis was found to be more common than thrombocytosis in pertussis.

Macrolide is the gold standard treatment for pertussis. A vast majority of our patients received the standard treatment with erythromycin ethylsuccinate, which has been studied to reduce the duration and severity of infections and shorten the duration of communicability among infected pertussis patients [1].

The study had the limitation of a cross-sectional design and was done as a single-centre study. Children with pertussis who presented with mild symptoms may lead to underdiagnoses and late presentations beyond catarrhal stage may lead to false-negative PCR testing. Furthermore, PCR testing was done in secondary centre making the diagnoses retrospective.

Findings from local epidemiological data foster the establishment of infectious disease database. Future aim to develop clinical management algorithm based on presenting symptoms and guide for appropriate clinical actions will benefit primary health centres to improve surveillance programmes. Hence, primary care liners should have a high index of suspicion when dealing with children presenting with cyanosis.

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