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Short Communication

Pertussis surveillance in a children hospital in Bangkok, Thailand

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ABSTRACT

Objectives: To investigate the incidence, clinical characteristics and cost associated with pertussis in Thai children with persistent cough.
Methods: A prospective study was conducted among children aged 0–18 years with persistent cough for ≥7 days with at least one of the following: paroxysm, inspiratory whooping, or post-tussive emesis. Nasopharyngeal swabs were obtained and tested for pertussis real time polymerase chain reaction (RT-PCR).
Results: 19.6% of children (28 out of 143) had pertussis confirmed by RT-PCR, 75% of cases occurred in children who were too young to complete their primary series of vaccine. Paroxysm and post-tussive emesis were the most consistent clinical features, identified in 96% and 93% of cases, respectively, whooping was found in only 18%. Pertussis cases were more likely to have household cough contact (64% versus 30%, $p < 0.001$), be hospitalized (79% versus 58%, $p = 0.048$) and experience protracted duration of cough (47 vs. 20 days, $p < 0.001$) compare to their counterpart.
Conclusion: Pertussis in Thai children is not infrequent and the common age group is young infant before completion of primary series of pertussis vaccine at six months of age, underline the importance of maternal pertussis immunization.

Introduction

Prevention for pertussis in young infants is unacheivable through child immunization alone, urging pregnant women to receive vaccination in developed countries (Amirthalingam et al., 2014). In developing countries such as Thailand, data on pertussis burden in children is lacking to support a maternal immunization policy regarding pertussis (Forsyth et al., 2012). A modeling study has demonstrated a long duration of pertussis immunity in Thai population (Blackwood et al., 2013), whereas as much as 18% of Thai adults with prolonged cough had documented pertussis in a serological study (Siriyakorn et al., 2016). Recommendation of pertussis vaccines for Thai pregnant women justifies more information apart from the country routine disease report, in which pertussis in infants could go underrecognized. We conducted surveillance at Queen Sirikit National Institute of Child Health, the largest public children hospital in Thailand to investigate PCR-confirmed pertussis in Thai children.

Materials and methods

From March 2011 to September 2013, we prospectively enrolled children presented at the outpatient clinic with cough for ≥7 days with at least one of the followings; paroxysm, inspiratory whooping, or post-tussive vomiting. Because of atypical pertussis presentations in young infants, all children aged ≤6 months who coughed ≥7 days were enrolled. Children diagnosed with asthma, tuberculosis or foreign body aspiration were excluded.

We collected patients' information including vaccination history and obtained a nasopharyngeal swab for pertussis real-time polymerase chain reaction (RT-PCR) (Farrell et al., 2000). Enrolled children were followed by telephone contact once a week until symptoms resolved to obtain information on their medical and travel costs, and disease outcomes.

The statistical analysis was performed using SAS, version 9.4 (SAS Institute Inc., Cary, NC, USA). A p-value < 0.05 was considered statistically significant.

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Results

One-hundred and forty-three patients were enrolled, 15 (10.5%) aged less than 2 months, 44 (30.8%) between 2 to 5 months, 26 (18.2%) between 6 to 12 months, 43 (30.1%) between 1 to 5 years, and 15 (10.5%) between 6 to 18 years. Almost all except four children provided their vaccination records, overall 5.8% did not receive the combined diphtheria-tetanus-pertussis vaccine (DTP) per the country Expanded Program on Immunization (EPI) (primary series at 2, 4, and 6 months, booster at 18, 48 months and 11-12 years of age). The incidence of PCR-confirmed pertussis in children seeking medical care for severe cough $\geq$7 days was 19.6% (95% CI 13.9, 26.8).

Children with PCR-confirmed pertussis were significantly younger; median age was 2.8 months (IQR 2.1, 9.8) ($p < 0.001$), 75% were less than 6 months of age. Sixty-four percent had a household member who coughed 1-3 weeks before the patients developed symptoms; the members were grandmothers (5), mothers (5), older siblings (4), fathers (2), grandfathers (2), and a non-relative member. Almost all children with PCR-confirmed pertussis had paroxysmal cough and post-tussive vomiting (96.4% and 92.9% respectively) while a whooping characteristic was not common (17.9%). We observed cyanosis in half of the children with pertussis and it was significantly more common compared to those with negative pertussis PCR ($p < 0.001$), (Table 1).

All patients recovered, children with PCR-confirmed pertussis experienced significantly longer duration of cough than those with negative PCR (46.6 days (SD = 18.7) versus 20.2 days (SD = 11.6), $p < 0.001$). A higher proportion of PCR-confirmed pertussis patients also required hospitalization compared to those with negative PCR (78.6% versus 58.3%, $p = 0.048$). The length of stay and direct cost did not significantly differ between the two groups. Table 2 demonstrates characteristics of pertussis patients, three-fourths received less than 3 doses of DTP. Seven patients received macrolide antibiotics before enrollment. Medical costs of pertussis patients were less than 100 USD among children who did not require hospitalization but much higher for those hospitalized.

Discussion

Our findings suggest a high incidence of PCR-confirmed pertussis among Thai children presenting with prolonged cough. Most pertussis patients were under six months of age and did not complete the primary DTP vaccine series when they contracted pertussis. Also, the precedent history of household members coughing was significantly higher in pertussis patients. Of note, most suspected index household members reported weeks of coughing and took over-the-counter medicines without discovering the diagnosis, suggesting under-diagnosed pertussis in adults as well as in children.

Although the resurgence of pertussis has been reported in countries with high vaccination coverage resulting in severe disease in very young infants (Clark, 2014), data in developing countries is limited. Our study is the first study to demonstrate the considerably high incidence of pertussis in Thai infants despite following the country immunization program.

Several reasons for pertussis resurgence have been proposed including switching from whole-cell pertussis (wP) to acellular pertussis vaccine (aP) (van der Lee et al., 2018). In Thailand, only wP is used in the country immunization program, and the coverage of the primary series of pertussis vaccine is almost 100% (WHO/UNICEF, 2017). However, the coverage of the booster doses is not known. The short protection of immunity from primary series pertussis vaccines whether wP or aP and inadequate booster doses coverage may cause pertussis in adolescents or adults who can transmit pertussis to young infants.

The Royal Thai College of Obstetricians and Gynecologists has recommended diphtheria-tetanus-acellular pertussis (Tdap) vaccine during pregnancy, however, maternal immunization coverage among Thai population remains very low (Ditsungnoen et al., 2016). Increasing evidence of infants' protection effects from Tdap (Wanlapakorn et al., 2018) together with information on pertussis burden among Thai infants underlines the need to improve pregnant women's immunization strategies.

Table 1
Demographic, clinical characteristics, outcomes, and medical cost.

Characteristics	All (n = 143)	Pertussis PCR		P value
		Positive (n = 28)	Negative (n = 115)	
Median age in months (IQR)	8.1 (3.2–39.7)	2.8 (2.1–9.8)	10.4 (4.4–46.0)	<0.001
Male gender (%)	73 (51.1)	11 (39.3)	62 (53.9)	0.165
Following EPI schedule[a] (%)	131 (94.2)	26 (92.9)	105 (94.6)	0.662
Having a household member with cough 1–3 weeks prior to symptoms onset (%)	52 (36.4)	18 (64.3)	34 (29.6)	<0.001
Clinical signs and symptoms				
Fever	76 (53.1)	16 (57.1)	60 (52.2)	0.638
Paroxysmal cough	113 (79.0)	27 (96.4)	86 (74.8)	0.012
Post-tussive vomiting	103 (72.0)	26 (92.9)	77 (67.0)	0.005
Whooping sound	10 (7.0)	5 (17.9)	5 (4.4)	0.025
Difficulty breathing	74 (51.7)	16 (57.1)	58 (50.4)	0.526
Wheezing	42 (29.4)	10 (35.7)	32 (27.8)	0.413
Cyanosis	24 (16.8)	14 (50.0)	10 (8.7)	<0.001
Apnea	13 (9.1)	3 (10.7)	10 (8.7)	0.719
Total duration of cough in day (SD)	25.4 (16.9)	46.6 (18.7)	20.2 (11.6)	<0.001
Hospital admission (%)	89 (62.2)	22 (78.6)	67 (58.3)	0.048
Median direct healthcare cost in US dollars (IQR)	185.6 (33–445)	167.2 (83–458)	244.2 (22–444)	0.214

[a] 4 children did not have vaccination record.

Table 2
Case of pertussis.

Case	Age (months)	DTP vaccine dose received	Prior Antibiotics	Clinical diagnosis	Hospitalized (days)	Cost (USD)
1	0.9	0	Erythromycin	Pneumonia	19	865
2	1.5	1	None	Pneumonia	3	124
3	1.6	0	Erythromycin	Bronchitis	8	249
4	1.6	0	None	Pneumonia	6	390
5	1.6	0	None	Pneumonia	5	257
6**	1.9	0	None	Bronchiolitis	19	2582
7	2.0	0	Erythromycin	Pneumonia	3	83
8	2.1	0	Amoxycillin	URI	4	210
9	2.1	0	None	URI	7	461
10	2.4	0	Erythromycin ceftriaxone	URI	10	454
11	2.4	0	None	Bronchiolitis	7	239
12	2.5	1	None	Bronchiolitis	9	277
13	2.7	0	Erythromycin	Bronchiolitis	9	445
14	2.8	1	None	Bronchiolitis	3	163
15	2.8	0	Azithromycin cefotaxime	Pneumonia	27	1198
16	2.9	0	None	Bronchiolitis	14	662
17	3.3	0	None	Bronchitis	8	396
18	3.6	1	None	Bronchiolitis	2	107
19	5.5	2	None	URI	0	47
20	5.9	2	Ampicillin	Bronchiolitis	11	655
21	6.2	2	None	Pneumonia	0	40
22**	13.3	3	None	Pneumonia	15	471
23	14.8	3	None	URI	0	33
24	17.7	3	None	Bronchiolitis	5	220
25	22.7	3	None	URI	0	5
26	30.4	4	Azithromycin	Pneumonia	4	40
27	45.5	4	None	Bronchitis	0	30
28	47.0	4	None	Bronchitis	0	83

*URI-Upper Respiratory Tract Infection. **Co-infection-The patient#6 was co-infected with Respiratory syncytial virus (RSV) and the patient#22 with *Streptococcus pneumoniae.*

Competing interest

All authors declare that they have no competing interest.

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Ethical approval

The study has been approved by the Queen Sirikit National of Child Health Research Ethic Committee.

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