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Bonus RB, et al. Clinical Profile of Pertussis Patients at PGH

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The authors declare that the data presented are original material and have not been previously published, accepted or considered for publication elsewhere; that the manuscript has been approved by all the authors, who have met the requirements for authorship.

ORIGINAL ARTICLE

CLINICAL PROFILE OF PERTUSSIS AMONG PEDIATRIC PATIENTS ADMITTED AT THE PHILIPPINE GENERAL HOSPITAL

ABSTRACT

Objective: The aim of this research was to describe the epidemiologic, clinical, laboratory and microbiologic characteristics, complications and outcome of pertussis among pediatric patients at the Philippine General Hospital

Methods: A retrospective chart review was performed which included pediatric patients with final diagnosis of pertussis, both clinical and laboratory-confirmed, admitted from December 2012 to August 2013 at the Philippine General Hospital.

Results : This chart review included 28 pertussis patients highest in those aged 1-3 months (86%), females (57%) and from region 4A (57%). 26 (93%) had exposure to household members with respiratory symptoms and unknown pertussis vaccination status. Of those patients who were eligible for vaccination, only 24% received age-appropriate DPT vaccination.

Onset of illness varied from 3-56 days; majority <2 weeks (57%). The following symptoms were observed: paroxysmal cough (100%), cyanosis (100%), fast breathing (93%), post-tussive vomiting (32%), fever (25%), and apnea (11%). None of patients presented with classical whoop. All patients had leukocytosis (mean WBC: $56.14x10^9$/L, range: $14.7\text{-}111.5x10^9$/L;), lymphocytic predominance (mean lymphocyte 0.47, range: 0.20-0.72;) and thrombocytosis (mean platelet count: $567x10^9$/L, range: $269\text{-}823x10^9$/L;). 28% were culture positive for *B. pertussis*, while 86% tested positive for PCR.

The most common complications were pneumonia requiring mechanical ventilation (64%), ARDS (28%), seizures (21%), nosocomial pneumonia (11%) and myocarditis (11%). The average length of hospital stay was 7.4 days with 13 deaths or 46% case fatality rate. Deaths were attributed to respiratory failure due to progressive pneumonia and ARDS. Other contributing causes were arrhythmia, MODS, and septic shock.

Conclusion: Susceptible young infants acquire pertussis from household contacts with respiratory symptoms. Paroxysmal cough and cyanosis are common clinical features, with leukocytosis, lymphocytosis and thrombocytosis. High case fatality rate for pertussis was noted among these patients.

KEYWORDS:
Bordetella pertussis, pertussis, DPT vaccination, pertussis pneumonia, whooping cough

INTRODUCTION

Bordetella pertussis is a highly contagious gram-negative coccobacillus that is an exclusive human pathogen[1]. It has a wide spectrum of clinical manifestations ranging from asymptomatic infection in children and adults with strong immunity to a more severe and life-threatening disease in unprotected newborns[2]. Pertussis in our country showed cyclic increases in incidence; this peaked in 2009 with 91 reported cases. The case fatality rate ranged from 2.2% to 5.3% between 2008 to 2012[3]. In the Department of Pediatrics of the Philippine General Hospital, the number of patients with suspected signs and symptoms of pertussis increased sharply in December 2012. This was in parallel with the reported cases to Department of Health on February 25, 2013 (Morbidity Week 8), with 33 cases and 18.2% case fatality rate[3].

The diagnosis of pertussis is difficult to ascertain from a clinical perspective because of the heterogeneity in disease manifestations, modification of disease by immunization, mixed infections and a low index of suspicion among physicians. The increased number of pertussis cases prompted to explore this vaccine-preventable disease in order to improve understanding among clinicians so that prompt medical and supportive care can be administered.

The general objective of this study is to determine the epidemiologic, clinical, laboratory and microbiologic characteristics, complications and outcome of pertussis in pediatric patients admitted at a tertiary medical center from December 2012 to August 2013. Specifically, to describe the epidemiologic features (age, gender, geographic distribution, exposure history, and vaccination status); to describe the clinical characteristics (onset of illness prior to admission and clinical manifestations); to describe the laboratory (complete blood count and chest radiograph findings) and microbiologic (nasopharyngeal swab for pertussis PCR and pertussis culture and culture studies of blood and endotracheal aspirate); and to describe the complications and outcomes of pertussis patients

MATERIALS AND METHODS:

A chart review of all pediatric patients 0 to 18 years old with clinical impression of pertussis was conducted at a tertiary medical center from December 1, 2012 to August 31, 2013. Pertinent patient data as to epidemiologic, clinical, laboratory and microbiologic characteristics were obtained. Initial laboratory findings on WBC, lymphocyte and platelet counts as well as the chest radiographs were included. Results of the nasopharyngeal swabs for pertussis PCR and culture which were sent to the national reference laboratory as well as cultures of blood and endotracheal aspirates were collected. The outcome and complications during hospitalization were noted. Patients with final diagnosis of pertussis, both clinical and laboratory-confirmed, were included in the analysis.

This study was undertaken in compliance with the Principles of the Declaration of Helsinki. Ethics approvals was sought and given by the University of the Philippines Ethics Review Board prior to initiation of the study.

All data were entered into a Microsoft Excel database. Descriptive analysis was performed and odds ratio on DPT vaccination, onset of illness, pertussis PCR and pertussis culture were computed.

RESULTS

Thirty one patients were admitted with impression of pertussis. However, three were excluded because of clinical and laboratory findings consistent with tuberculosis. Twenty-eight patients were included in the case series.

Table 1. Epidemiologic Features of Pertussis Cases

	n = 28	%
Age group		
< 1 month	2	7
1-3 months	24	86
4-6 months	1	4
6-12 months	0	0
1-5 years	1	4
Median age (range) in months	**1.75 (0.75 – 53)**	
Gender		
Male	12	43
Female	16	57
Region		
4A	16	57
NCR	11	39
3	1	4

Table 1 shows the epidemiologic features of pertussis cases. The age range of patients varied from as young as 3 weeks up to 53 months, with a median age of 1.75 months. Majority of patients were female (57%). Figure 1 shows the geographic distribution of pertussis cases with the highest reported number in regions 4A (n = 16, 57%) and NCR (n = 11, 39%).

Figure 1. Geographic Distribution of Pertussis Cases

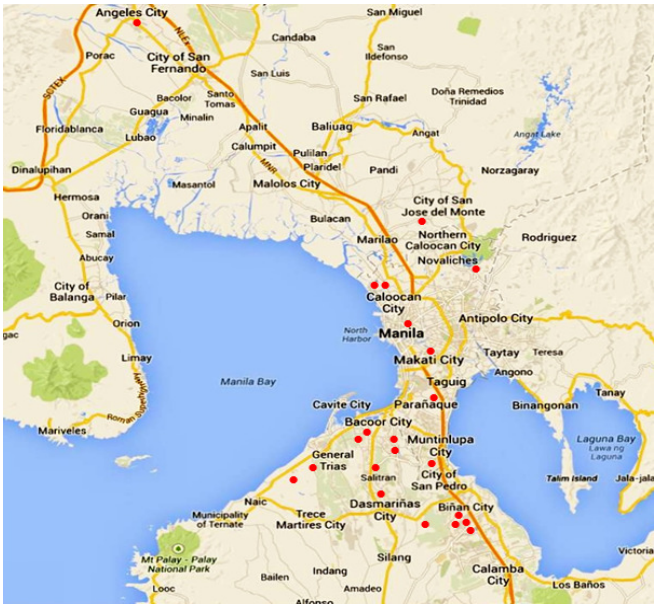

Table 2. Exposure History of Pertussis Cases

	n	%
Exposure history		
With exposure	26	93
No exposure	2	7
Number of Exposure (n = 26)		
Exposed to 1 sick household member	17	65
Exposed to > 1 sick household member	9	35
Identified sick household member (n = 34)		
Adult	9	
Mother	11	
Children		
< 5 years old	9	
5-18 years old	5	

Table 2 shows the exposure history of pertussis patients to sick household members. Most of them had exposure to a symptomatic household (93%) with nine patients (35%) exposed to more than one sick household member. On review, cough was the most common symptom of these contacts, who were mostly adults with unknown pertussis vaccination status. The mother was identified in 11 cases, also with unknown pertussis vaccination. Other significant exposures were siblings or cousins less than 5 years old (n=9), who on review had no booster doses for pertussis.

Vaccination Status of Pertussis Patients

Of the twenty-eight, 10 (36%) were not eligible to receive DPT vaccination because of age less than 6 weeks. Of those patients who are eligible for vaccination, only 5 (28%) received age-appropriate DPT vaccination. DPT was deferred in 13 patients because of the following reasons: cough (n = 8, 62%), temperature of 37.5°C (n = 2, 15%) and rash (n = 1, 8%). The remaining 2 patients were not brought to the health center at all for immunization due to lack of time.

Clinical and Laboratory Characteristics of Pertussis Patients

Table 3 shows the clinical characteristics of pertussis patients. In this series, the onset of

illness before admission varied from 3 to 56 days, with a median duration of 11 days. Fifty-seven per cent of infants were noted to be ill for less than 2 weeks. Pertussis patients presented with paroxysms of cough, accompanied by cyanosis and fast breathing. The characteristic whoop was not seen in any of the patients.

Table 3. Clinical Characteristics of Pertussis Patients

	N	%
Onset of illness in days		
Less than 2 weeks	16	57
2-4 weeks	8	28
4-6 weeks	2	7
6-8 weeks	2	7
Median onset of illness in days (range)	11 (3 to 56)	
Clinical Manifestations		
Paroxysmal cough	28	100
Cyanosis	28	100
Fast breathing	26	93
Post-tussive vomiting	9	32
Fever (T > 38°C)	7	25
Apnea	3	11
Whoop	0	0

As for the laboratory characteristics, All patients had leukocytosis (mean WBC: $56.14x10^9$/L, range: $14.7\text{-}111.5x10^9$/L ;), lymphocytic predominance (mean lymphocyte 0.47, range: 0.20-0.72 ;) and thrombocytosis (mean platelet count: $567x10^9$/L, range: $269\text{-}823x10^9$/L). Chest radiographic findings consistent with pneumonia were noted in 93% of cases.

Table 4 shows the microbiologic characteristics of nasopharyngeal swab for *Bordetella pertussis* polymerase chain reaction (PCR) and culture. PCR was tested positive in 24 (86%) patients, highest in aged 1-3 months. *B. pertussis* was isolated in 8 (28%) patients, also in the same age group. Ten patients (100%) were PCR positive if onset of illness occurred within 2-6 weeks.

There were no isolated organisms in all of the 21 blood specimens submitted. A total of 9 ETA specimens were collected which yield normal respiratory flora in 4 specimens. Isolated organisms include: *Pseudomonas aeruginosa* (2), *Acinetobacter baumanii* (2) and *Klebsiella ozanae* (1).

Table 4. Microbiologic Characteristics of Nasopharyngeal swab

	n = 28	PCR Positive n = 24		Culture Positive n = 8	
		n	%	n	%
Age group					
< 1 mo	2	0	0	0	0
1-3 mos	24	22	92	**8**	33
4-6 mos	1	1	100	0	0
6-12 mos	0	0	0	0	0
1-5 yrs	1	1	100	0	0
Onset of illness					
< 2 weeks	**16**	**13**	81	3	19
2-4 weeks	**8**	**8**	**100**	3	37
4-6 weeks	**2**	**2**	**100**	1	50
6-8 weeks	2	1	50	1	50

Nineteen patients (68%) required mechanical ventilation upon admission. Pneumonia progressed to acute respiratory distress syndrome in 32% and 7% developed nosocomial pneumonia. Other complications noted were seizures (21%) and myocarditis (11%). The average length of hospital stay is 7.4 days (range of 1 to 19 days).

Characteristics of Mortalities

The case fatality rate in the series is 46%. The median age of mortality was 7 weeks old (age range from 4 to 12 weeks); majority were female (54%).

Eleven patients (85%) did not receive DPT vaccination; 6 of whom were not eligible because of age less than 6 weeks. In the series, the probability of dying from pertussis was 1.4 (95%, CI 0.19-9.83) among unvaccinated patients.

Patients who died had onset of illness from 3 to 31 days with a median of 10 days. Majority of patients who died in this series had onset of illness less than 2 weeks and the probability of dying was 2.6 (95%, CI 0.54-12.17).

All mortality cases had laboratory features of leukocytosis with lymphocytic predominance and thrombocytosis. Twelve patients (92%) had chest x-ray findings consistent with pneumonia.

All patients who died were pertussis PCR positive. The probability of dying in those who are pertussis PCR positive is 5.8 (95% CI 0.59-57.10). Mortality cases had 31% positivity for *B. pertussis* on *NPS*. The probability of dying in those who are pertussis culture positive is 1.2 (95%; CI 0.24-6.31).

The most common complications noted were pneumonia requiring mechanical ventilation. Other complications include acute respiratory distress syndrome (61%), seizures (38%), myocarditis (23%) and nosocomial pneumonia (23%). Deaths were attributed to respiratory failure due to progressive pneumonia and ARDS. Other contributing causes were arrhythmia, multiple organ dysfunction syndrome (MODS), and septic shock.

DISCUSSION

During this case series, hospitalized patients due to pertussis included 28 infants and children highest in those aged 1-3 months (86%), females (57%) and from region 4A (57%). In comparison to the 2012 annual report of Philippine Disease Surveillance Report (PIDSR), a total of 76 suspected pertussis cases were reported[12]. As in the series, age group with the highest number of cases is less than 1 year old; majority were females. The report also showed that most cases were from NCR (23.68%), followed by regions 6, 7 and 4A[4] in contrast to the case series. The catchment area of our hospital does not include regions 6 and 7.

A study done during the 2010 pertussis epidemic in California noted infants less than 3 months of age hospitalized had household coughing contacts[5]. This was similar in this series who also noted the patient's mother and siblings as the usual contact.

In our country, the recommended completion of the primary vaccination series is by six months. According to the recent estimates in 2012, coverage of the three-dose primary vaccination varies widely from as low as 66% in India to as high as 99% in Thailand. The Philippines' DTP3 coverage has increased to 87% from 80% (2011)[6]. Despite noted increase in the DTP3 coverage, pertussis continues to rise in our country. Based on the series, the most affected age group were not eligible to receive the vaccine and even if they were vaccinated, a single dose of vaccine will not adequately protect them from pertussis. Exposure to an adult or their siblings without booster doses on pertussis contributed to the number of cases by serving as a reservoir of infection and source of transmission to these infants. Thus, blocking this transmission by immunizing the household contacts is important in pertussis control.

The results in this series indicate several features that should alert clinicians to pertussis, including paroxysmal cough, cyanosis, fast breathing, post-tussive vomiting, apnea and absence of fever. The classical whoop was not seen. Onset of illness varies from 3 to 56 days; majority less than 2 weeks. This is in contrast to the WHO and CDC clinical definition of pertussis on the basis of cough illness for more than two weeks with at least one of the following condition like paroxysms, whooping cough, and post-cough vomiting without other apparent causes. The clinical presentation is often difficult to observe by parents and even medical personnel causing a delay in consult, diagnosis and treatment. It is noteworthy that probable

pertussis should be consider in young infants with paroxysms of cough associated with perioral cyanosis, post-tussive vomiting, afebrile, having no DPT immunization and had household coughing contacts.

Physicians who have diagnosed patients with a probable pertussis can be guided by laboratory findings such as leukocytosis and absolute lymphocytosis. Severe leukocytosis with pulmonary hypertension is associated with increased risk of mortality. In a case series of 13 infants with pertussis, hyperleukocytosis (>100 x 10^9/L) was an independent predictor of death[7]. The disease severity was via the formation of aggregates in the pulmonary vasculature. Therapeutic approaches include leukocyte-reducing measures[8]. However, more data are needed. In this series, hyperleukocytosis were seen in 3 infants who all expired.

PCR results were positive in 86% of assays done; culture results were positive in 22% done. No patient with negative PCR results had a positive result for culture. The timing of PCR testing for pertussis can affect its ability to accurately diagnose the disease. PCR has optimal sensitivity during the first 3 weeks of cough when bacterial DNA is still present in the nasopharynx. After the fourth week of cough, the amount of bacterial DNA rapidly diminishes which increases the risk of obtaining falsely-negative results. Culture is the gold standard however, positive culture of B. pertussis is difficult to be obtained as the test may be affected by specimen collection, transportation, and isolation techniques. Higher isolation result is obtained during the catarrhal and early paroxysmal stages, two weeks during course of illness, with its positive variation of 30%–50%[9].

In this study, the most common complications noted were pneumonia requiring mechanical ventilation, acute respiratory distress syndrome, seizures, nosocomial pneumonia and myocarditis. Results were similar in a multi-center prospective cohort study on the acute course of critical pertussis in pediatric intensive care units in the United States with a total of 127 patients identified. The cohort reported complications such as development of pneumonia, pneumothorax, bradycardia, hypotension, pulmonary hypertension, abnormal bleeding, CNS bleed and seizure[10]. There were 12 deaths with 9.4% case fatality rate attributed to pulmonary hypertension and cardiac arrest. This was lower as compared in this series' 46% case fatality rate.

CONCLUSIONS

In spite the EPI, 31 cases of pertussis were reported and most were susceptible young infants acquire pertussis from household contacts with respiratory symptoms. Most common clinical features were paroxysmal cough and cyanosis, with leukocytosis, lymphocytosis and thrombocytosis. The classical whoop was not seen in these patients. A high case fatality rate for pertussis was documented.

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