



Clinical Manifestations of Probable Pertussis in Pediatrics Admitted to Bandar Abbas Children' Hospital

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ABSTRACT: Pertussis is a highly contagious respiratory disease that children are being vaccinated in our country for prophylaxis. Despite high vaccination coverage the incidence of pertussis is still increasing. This study was done to investigate the prevalence of pertussis in children and its clinical manifestations before and after the beginning of vaccination age. This descriptive-analytic study was performed in children with coughs for more than two weeks whom found with no reason for prolonged cough and were diagnosed with pertussis. The clinical records of the patients were assessed and the result of culture was studied. The data was then analyzed using chi square test in SPSS. A total of 140 patients including 77 (55%) male and 63 (45%) female with the mean age of 5.19 ± 3.13 months enrolled in this study that had history of more than two weeks cough. There was no significant difference in clinical manifestations of the two groups (less and more than six months). It is suggested to vaccinate mothers for immunization of children.

Key words: Pediatric, Pertussis, Clinical manifestations

ORIGINAL ARTICLE

INTRODUCTION

Pertussis, or whooping cough, is a highly contagious respiratory disease caused by *Bordetella pertussis* or *B. parapertussis*. High levels of vaccination coverage have been achieved in infants and toddlers in world, and infant morbidity and mortality have significantly reduced. The annual worldwide incidence of pertussis is estimated to be 48.5 million cases, with a mortality rate of nearly 295,000 deaths per year (Thompson, 2010). The case-fatality rate among infants in low-income countries may be as high as 4% (Nitsch-Osusch, 2013). In Iran, a steady decline in the incidence rates after the introduction of vaccination since 1984 was similarly observed (CDC, 2009). After 2001, the annual pertussis incidence among persons aged 10-19 years steadily increased in the United States and in Iran it has increased since 2007 (Nakhost Lotfi, 2012).

Classically, pertussis is a 6-8 wks. disease, divided into catarrhal, paroxysmal, and convalescent stages. The catarrhal stage begins after an incubation period ranging from 1-3 weeks with non-distinctive symptoms of congestion and rhinorrhea. Then coughing marks the onset of 2-4 week of the paroxysmal stage. As paroxysmal stage fades into the convalescent stage, the number, severity, and duration of episodes diminish (Wilbert, 2011). Manifestation in infants is usually catastrophic. Severe pertussis leads to critical pertussis may manifest fatal for infants under three months of life because the symptoms may present themselves as other causes of illness such as

sepsis, very severe pneumonia, and encephalopathy, which may result in respiratory and cardiovascular disturbances (Burr, 2011). Pertussis may likely be misdiagnosed in its initial or catarrhal phase as a common respiratory infection (Nataprawira, 2013). The clinical diagnosis must be confirmed by specific laboratory tests, culture, serology, and polymerase chain reaction (PCR). The serology method had poor sensitivity and specificity. Culture is very specific, but its sensitivity depends on the culture conditions, as a result, culture sensitivity is low even under optimal technical conditions. Recent studies suggest that PCR based assays and real-time PCR-based assays are more sensitive than culture for detection of *B. pertussis* in nasopharyngeal specimens (Chia, 2004). A confirmed pertussis diagnosis is so difficult which leads World Health Organization (WHO) and Center of Disease Control and Prevention (CDC) to define pertussis cases as probable and confirmed (CDC, 2010; WHO, 2001). The aim of this study was to identify the demographic, clinical and laboratory characteristics in children with probable pertussis.

MATERIALS AND METHODS

A retrospective study of 140 probable pertussis patients was performed in the Department of Pediatric Infectious Diseases, Bandar Abbas Children's Hospital, 2011. A probable case was described as a case that meets the clinical case definition (cough illness lasting at least 2

weeks with one of the following: paroxysms of coughing, inspiratory “whoop”, or posttussive vomiting, without other apparent cause like cystic fibrosis, sinusitis, asthma, gastroesophageal reflux, foreign body, etc.) and is epidemiologically linked directly to a case, especially if the followings are absent: fever, malaise or myalgia, exanthema or exanthema, sore throat, hoarseness, tachypnea, wheezes, and rales. Apnea or cyanosis (before appreciation of cough) is a clue in infants <3 mo of age. Medical records of the patients were reviewed with respect to age, gender, pertussis vaccination status, paroxysmal cough, duration of the cough, cough with inspiratory whoop and/or cyanosis, cough ending in apnea or vomiting, findings on physical examination, and results of laboratory tests. To evaluate the household contacts of the index cases, family medical history of each patient was reviewed. Household contacts of the index cases had been considered as persons who were living in the same residence and had acute cough illness during the month preceding the pertussis diagnosis of the infant. To evaluate the acute phase reactants, the patient’s laboratory data [complete blood count (CBC) with differential, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP)] were collected upon admission to the hospital. Median leukocyte, lymphocyte and thrombocyte counts were compared between patients. According to our Pediatric Infectious Disease Department protocol for management of pertussis, patients' ≤6 months of age with suspected pertussis were hospitalized. All patients who had been suspected for having pertussis clinically were started on macrolides treatment. Data were entered into a

database, and statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS).

RESULTS

A total of 140 probable pertussis patients were included in the study. 77 (55%) of the patients were boys and 63 (45%) were girls. The mean age of the patients was 5.19 ± 3.13 months (range: 30 days-10 years). Seventy six patients (54.3%) were <6 months of age, and 60% of them were <6 months. All of the patients had a history of contact with a household member with respiratory symptoms. The number of the pertussis cases in this study is demonstrated in Table 1.

About 32.4% of the pertussis cases in the total study period occurred in spring, 32.1% in summer, 25.7% in autumn and 10.7% in winter. No patient had an underlying disease, and none was premature. Overall, at initial presentation, all of the patients had cough and clinical symptoms of the patients are summarized in Table 2.

The mean duration of cough was 12.4 ± 7.9 days (range: 20-35 days) that at <6 months of age was 3.7 ± 11 days and at above 6 months was $14 \pm 8/4$ days. Mean values and range of the WBC was $15814 \pm 11723/\mu\text{L}$ and $4300-93000/\mu\text{L}$, respectively and in 23.5% of them was above $20000/\mu\text{L}$. Mean values and range of the HB was 10.8 ± 1.4 g/dL and $6.7-15$ g/dL, respectively. Mean values and range of the Platelet was $351508 \pm 115034/\mu\text{L}$ and $109200-856000/\mu\text{L}$, respectively. Mean values and range of the ESR was 12.5 ± 10.8 and $3-75$ mm/L, respectively. Mean values and range of the laboratory tests of the hospitalized pertussis patients are presented in Table 3.

Table1: The number of the pertussis cases

Age	Percent	Number
Lesser than 6 month	54.3	76
7-24 months	27.1	38
25-72 month	15	21
More than 72 month	3.6	5
Total	100	140

Table 2: The prevalence of clinical symptoms

Clinical symptom	More than 6 months(percent)	Lesser than 6 months (percent)
Posttussive vomiting	57	44.4
Fever	39	27.2
Rhinorrhea	18.6	12.3
Whoop	3.4	3.7
Paroxysm	3.4	2.5
Apnea	0	2.5

Table 3: The laboratory tests of the hospitalized pertussis patients

Variables	Lesser than 6 months (76 person)	More than 6 months(64 person)	p-value
Hb	10.6 ± 1.4	11.11 ± 0.3	0.01
Platelet	349101.2 ± 117504.5	354813 ± 112470.9	0.77
WBC	13700 ± 6646.7	18716.1 ± 15924.9	0.01
Lymphocyte	50.6 ± 12.7	4.8 ± 10.7	0.7
ESR	12.2 ± 11	13.1 ± 10.6	0.63

DISCUSSION

Routine immunization against pertussis began in Iran in 1984 with whole cell diphtheria-tetanus-pertussis (DTwP) vaccination for the primary (at 1.5, 3, 4.5 months of age) and booster doses (at 18 month of age), and the coverage rates reached above 90% and then changed (at 2, 4, 6 months of age). Despite this widespread vaccination practice in our country, infants <2 months of age are still unprotected from pertussis. For this reason, most of the patients in this study were young infants who had not yet been vaccinated. Family members with undiagnosed and unrecognized pertussis are the major source of pertussis in infants. Studies have shown that parents, especially mothers, are the source of disease transmission. According to a retrospective survey of the records of the Iranian Ministry of Health, reported pertussis cases since 2007 were increased (CDC, 2009).

In our study, most patients were infants <6 months of age and most patients had a history of contact with a family member who was coughing that their diagnosis has not taken. Maternal antibody and its effect on protection were not identified. In a study by Saffar found that maternal antibody against pertussis were low to help their infants and, at least, protects severity and complications (Saffar, 2008). It has been known that, despite the widespread vaccine practice, the pertussis epidemiological cyclic pattern has not changed. (Harnden, 2006; Zarei, 2007) The seasonality of pertussis and age-specific long-term periodicity in the Netherlands were investigated over a 10-year period. They found the highest incidence for all age groups to be in August, and in a Canadian study, the peak incidence of hospitalizations for pertussis occurred between July and September each year during a seven-year period. On the other hand, in another study from Germany, cases of pertussis were diagnosed with equal frequency during both the warm season from April to September (47.2%) and the colder season from October to March (52.8%) over the six-year study period (De Greeff, 2009; Halperin, 1999; Heininger, 1997).

In our study most patients were seen between springs to autumn, but the current study was a clinical case series, not an epidemiological study. In our study 55% of patients were boys that were compatible with many other studies (Edelman, 1996; CDC, 2012).

In a large study that described the features and outcomes of neonatal pertussis, the presentation symptoms according to frequencies were reported as cough, cyanotic spell, paroxysmal cough, equally apnea and rhinorrhea/congestion, tachypnea, and fever (Castagnini, 2010). In our study, there were lesser symptoms. None of them required invasive or noninvasive mechanical ventilation. We thought that they had been given appropriate antibiotics and supportive care early in the illness. In our study, posttussive vomiting was about 50% that in other studies the range were 57%-67 % (Edelman,

1996; CDC, 2012; Castagnini, 2010) in our study, paroxysmal cough was 6% that is lesser than other studies that may be due to incorrect recording. (Edelman, 1996; CDC, 2012) In our study, apnic spell was 2.5% that all of them were ≤ 6 months and whoop was 7% that in other studies the results were heterogenic. (CDC, 2012; Castagnini, 2010; Kösters, 2001, www.saglik.gov, 2012; Wendelboe, 2007) Fever is not an expected finding of pertussis that in our study was 32.1% (Tabatabaei, 2009; Long, 2009)

The principal complications of pertussis are apnea, secondary infections (such as pneumonia and otitis media), respiratory failure (apnea, pneumonia, or pulmonary hypertension), physical sequelae of forceful coughing (rib fracture, conjunctival bleeding, and inguinal hernia), seizures, encephalopathy, and death (Wymann, 2011) that in our study it was at least and we have only 2 cases of otitis media ,may be due to hospitalization and early antibiotic therapy. The reported rate of pneumonia varies from 1.7- 9.4 % (Namachivayam, 2007). However, we have no pneumonia in our study. Pertussis is a toxin-mediated disease associated with several virulence factors, including pertussis toxin, has multiple proven biological activities, like leukocytosis and lymphocytosis. Leukocytosis attributable to lymphocytosis is a hallmark of pertussis infection. It has been reported that severe or fatal pertussis is correlated with the degree of lymphocytosis (Mikelova, 2003) the majority of our patients had significant lymphocytosis and thrombocytosis that have no compatibility with severity of disease and only supported the diagnosis.

Although the largest increase in pertussis cases has been among adolescents and adults, the annual reported incidence has been highest among infants younger than 1 year. (Mattoo, 2005) Because of the lack of maternal immunity transfer, 10-15% of all cases of pertussis occur in infants younger than 6 months; more than 90% of all deaths occur in this same age group. Neither acquisition of the disease nor vaccination provides complete or lifelong immunity. Protection against typical disease wanes 3-5 years after vaccination and is not measurable after 12 years. (Winter, 2010) However, the growing majority of cases are now in persons aged 10 years and older, which has led to increased booster recommendations (Bisgard, 2000).

Ultimately, despite extensive vaccination efforts, pertussis incidence has cyclically increased in Iran. Vaccination does not provide complete or lifelong immunity; therefore, we recommend the proper vaccination coverage of mothers and if possible use the cellular vaccines to mothers and adult population, as an index case for kids. Additionally, we recommend hospitalization of patient's ≤ 6 months of age with suspected pertussis, regardless of the disease severity, and

treatment with macrolides and supportive measures without waiting for PCR and culture results. According to the finding of this study as well as the lack of easy access to rapid and specific diagnostic techniques, we advise to do the broader studies using diagnostic procedures and reviews of subsequent complications.

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