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Evaluation of clinically suspected pertussis in children attending Rapareen Teaching Hospital in Erbil Governorate

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Abstract

Background and objective: Pertussis is one of the vaccine preventable diseases. Bordetella pertussis (B. Pertussis) continues to circulate even in countries with good childhood vaccination. The aim of this study was to evaluate patients suspected or confirmed to have pertussis in relation to certain clinical and laboratory data.

Methods: A prospective study was conducted in Rapareen Teaching Hospital from June 1st, to September 1st, 2010. The study enrolled 651 inpatients below five years of age with respiratory tract infection with 72 of them having initial suspicion of pertussis. Demographic and clinical data were obtained from them and nasopharyngeal swab were sent for culture for isolation of microorganisms as well as blood samples obtained for haematological assessment (white blood cell differential count and platelet count). Those confirmed to have pertussis and para-pertussis were considered as group A while other culture results were considered group B.

Results: Most of patients were below one year of age (56.9%) with large numbers were not properly vaccinated and they had positive family history of paroxysmal cough (68.1% and 58.3%, respectively). Twenty one patients confirmed to have pertussis and parapertussis by culture methods. There was no significant difference between patients with group A when compared to group B regarding gender, vaccination status, history of post-tussive vomiting or whoop and family history of chronic cough. Mean platelet count was significantly different between two groups, with pertussis and parap-pertussis cases had less platelet count.

Conclusion: Near half of patients with B. pertussis and parapertussis have a defect in their vaccination program.

Keywords: Pertussis, Culture, Cough, Patients.

Introduction

Bordetella pertussis is the causative agent of pertussis, also called whooping cough or cough of 100 days. With the advent of vaccines, the incidence of disease declined dramatically into 1970s, however, pertussis is still present, with peaks every 3-5 years.[1] Pertussis is one of the vaccine preventable diseases that can potentially be fatal. Despite the availability of a vaccine, the disease continues to pose a significant risk to infants. The case fatality varies but generally ranges between 2-3% in infants.[2] Among the diseases for which universal childhood vaccination has been recommended, pertussis is the least well-controlled reportable bacterial disease in the United States. Infants aged <12 months with pertussis are more likely than older age groups to have complications or be hospitalized during their illness.[3] In Iraq pertussis continues to occur throughout the country with high incidence (2312 reported cases in 2001).[4] In 1996, an epidemic occurred in Basra from June to December with 40% of those affected were under five years.[5] The clinical course of illness is divided into three stages;

• The catarrhal stage is characterized by the onset of runny nose, sneezing, low-grade fever, and a mild cough. Cough gradually becomes more severe and after

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1-2 weeks the next stage develops.

• The paroxysmal stage is characterized by coughing fits (paroxysms), which may be followed by a high-pitched inspiratory whoop, vomiting, and/or apnea. This stage usually lasts 1-6 weeks

• The convalescent stage is characterized by fewer paroxysmal coughing episodes and usually disappears in 2-3 weeks, but may continue for months.[6]

The most frequent complication observed in children is pneumonia. Other complications include sinusitis, otitis media, viral and bacterial superinfections, nutritional deficiencies and neurologic complications, which are due mostly to hypoxia during coughing spells.[2] The aim of this study was to evaluate patients suspected or confirmed to have pertussis and its relation to the clinical and laboratory data.

Methods

Study design and patients:

A prospective study was conducted on 651 patients below age of five years presented with respiratory tract infection admitted in Rapareen Teaching Hospital; which is the only pediatric hospital in Erbil city, Iraq. Seventy two patients with paroxysmal or prolonged cough with initial suspecion of pertusiss were included in this study during the period of three months (from June 1st, to September 1st, 2010) when outbreak of pertussis in population of different age groups was reported. Newborns, patients with chronic lung disease and those with underlying chronic illness were excluded from the study. A written consent was obtained from the proxy of patients and the study was approved by the Research Ethics Committee of the College of Medicine of Hawler Medical University. A questionnaire prepared by research team including sociodemographic and clinical data was used to interview the parents and caregivers for obtaining these data. Cases were classified according to clinical criteria to be:

1. Confirmed:

a. A positive culture for B. pertussis and an acute cough illness of any duration, or

b. Meets the clinical case definition and is confirmed by Polymerase chain reaction (PCR), or

c. Meets the clinical definition and is epidemiologically linked directly to a case confirmed by either culture or PCR.

2. Probable: A case that meets the clinical case definition, is not laboratory confirmed, and is not epidemiologically linked to a laboratory-confirmed case; also includes cases meeting the outbreak case definition.

3. Suspect: a clinical syndrome compatible with pertussis; an illness consistent with pertussis and without other apparent cause, such as:

a. Cough of ≥ 7 days, or

b. Paroxysmal cough of any duration, or

c. Cough with inspiratory whoop, or

d. Cough associated with apnea in an infant, or

e. Cough in a close contact of a confirmed or probable case [6].

Patients who had received the vaccine doses corresponding to their age were considered correctly vaccinated according to age. Patients who had received some doses of vaccine but not the correct number of doses were considered partially vaccinated. Unvaccinated patients were those who did not received any vaccine.[7]

Nasopharyngeal swab was obtained from 72 patients by research members. However, this number may represent only a small portion of the outbreak as there were many patients during the outbreak who were not included in the study.

Laboratory diagnosis:

Nasopharyngeal swabs were obtained and the specimens were collected in Charcoal Cephalexin Blood Agar (CCBA) media as transport media. The samples were cultured on Bordet Gengou (BG) within 4 hours. Bordet Gengou (BG) media was freshly prepared (not more than 10 days for BG or one month for CCBA) supplemented with cephalexin. Two milliliters of blood from each patient sent for hematological assessment (White cell and

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Platelet count). Those confirmed to have pertussis or parapertussis were considered as Group A while other culture results (other bacteria, fungal or no microorganisms) were considered Group B.

Statistical analysis:

Data were analyzed by the statistical package for the social sciences (version 18) using Chi square for categorical data and independent t test for comparing the mean of two groups. Fisher's exact test was used for small sized samples in the case of a 2 × 2 contingency table when Chi square test was not suitable. *P* value of ≤0.05 was considered to be significant.

Results

Most of patients included in this study were below the age of one year especially the first three months of life with male:female ratio 1.18; 39 male(54.2%) compared to 33 female (45.8%). A large number of them were not or improperly vaccinated (49 out of 72, 68.1%) and 16 of those confirmed to have pertussis or parapertussis were either unvaccinated (10, 47.6 %) and partially vaccinated (6, 28.6%) with no significant difference. Of 72 patients, only 21 confirmed to have pertussis and parapertussis (Figure 1) and there was no significant difference between patients with group A (pertussis and parapertusiss) according to culture when compared to group B (other microorganisms or no microorganisms) regarding gender, age, vaccination status, history of post-tussive vomiting or whoop and family history of cough for more than three weeks in first degree relatives (Table 1).

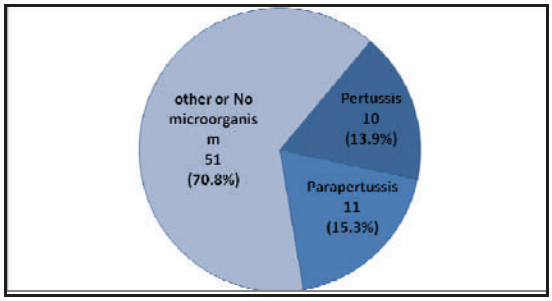

Figure 1: Culture results of 72 patients included in the study.

Table 1: Differences in obtained demographic and clinical variables between 2 groups (pertussis/parapertussis compared to other microorganisms/no microorgansims).

Variables		Group A n=21(%)	Group B n=51(%)	Total n=72 (% of total)	*P* value	OR (CI)
Gender	male female	12 (30.8) 9 (27.3)	27 (69.2) 24 (72.7)	39 (54.2) 33 (45.8)	0.75	1.19 (0.43-3.30)
Age	≤ 1 year > 1 year	14 (34.1) 7 (22.6)	27 (65.9) 24 (77.4)	41 (56.9) 31 (43.1)	0.28	1.77 (0.61-5.1)
Vaccination Status	Vaccinated Not or Partially vaccinated	5 (21.7) 16 (32.7)	18 (78.3) 33 (67.3)	23 (31.9) 49(68.1)	0.34	0.57 (0.18-1.82)
Post-tussive Vomiting	Yes No	16 (29.1) 5 (29.4)	39 (70.9) 12 (70.6)	55 (76.4) 17 (23.6)	0.98	0.99 (0.29-3.25)
Post-tussive Whoop	Yes No	13 (29.5) 8 (28.6)	31 (70.5) 20 (71.4)	44 (61.1) 28 (38.9)	0.93	1.05 (0.37-2.98)
Family hx of Paraxysmol cough	Yes No	12 (28.6) 9 (30.0)	30 (71.4) 21 (70.0)	42 (58.3) 30 (41.7)	0.89	0.93 (0.33-2.61)
Received Antibiotics	Yes No	21 (100.0) (0)	48 (94.1) 3 (5.9)	69 (95.8) 3 (4.2)	0.25	0.69 (0.59-0.81)

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Mean platelet count differed significantly between the two groups with Group A having less mean platelet count and *P* = 0.05 support such association while other variables were not significant when compared between the two groups but confirmed Group A cases were more among younger aged children. Surprisingly, Lymphocyte mean count was larger in number among Group B (Table 2).

Discussion

This study analyzed the epidemiological characteristic of 72 hospitalized patient suspected or confirmed to have pertussis. A total of 39 (54.2%) of clinically suspected cases were male and 33 (45.8%) of cases were female although there was no significant difference in the frequency distribution among them, which this supported by a study from Al-Diwaniyah, Iraq.[8] This study found a trend towards higher attack rates in children younger than one year. A similar finding was reported by other researchers (53.3% in Catalonia, 77.2% in Spain, 53% in Babil, Iraq),[9-11] but only 32.4% of cases were under one year in Saudia Arabia.[12] The high proportion of cases of hospitalized children <1 year in our study (56.9%) might be a reflection of severity of pertussis among infants.[7] It has been reported that vaccine induced immunity wanes over time leading to increased vulnerability. However, the present study found cases of pertussis in children as young as one month old with most cases where in the first three months of age and this could reflect a lack of protective immunity, possibly due to antigenic differences between circulating strains and vaccine strains.[13] Isolation of Bordetella pertussis through nasopharyngeal culture is regarded as gold standard for the diagnosis of pertussis due to its very high specificity (100%). However, the sensitivity of the culture has been shown to be low and may vary depending on the immunity from past infection or from vaccination, the stage of disease, how the specimen is handled, the age of the patient and the effective antibiotic pretreatment prior to culture.[14] In this study, nasopharyngeal culture was the only laboratory test used to confirm the diagnosis. It is likely that more cases would have been confirmed if serology and polymerase chain reaction assays were available.[15] This may explain the result obtained in our study that only 13.9 % and 15.3% have confirmed to have pertussis and parapertussis by culture respectively, although our data were in harmony with what was reported byYildirim et al in Turkey,[14] by Baptista in Brazil[15] and by Hochwald et al in Israel,[16] and higher than that was found by Cengizet et al in Turkey.[17] The great interest that for years has been devoted to the whooping cough

Table 2: Independent t test compared means of two groups (pertussis/parapertussis compared to other microorganisms/no microorganisms) regarding laboratory findings.

	Culture	No.	Mean (± SD)	*P* value
WBC (cells per mm^3)	Others (Group B)	51	15392 (± 9023)	0.94
	Pertussis & para. (Group A)	21	15233 (± 6027)	
Granulocyte (cells per mm^3)	Others (Group B)	51	5090 (± 3160)	0.35
	Pertussis & para. (Group A)	21	5992 (± 4812)	
Lymphocyte (cells per mm^3)	Others (Group B)	51	9159 (± 6613)	0.42
	Pertussis & para. (Group A)	21	7944 (± 3373)	
Platelet (count /µL)	Others (Group B)	51	345000 (± 107452)	0.05
	Pertussis & para. (Group A)	21	294666 (± 74028)	

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disease by B. pertussis has led to less attention to the closely related species B. parapertussis. In our study 11 patients (15.3%) yielded B. parapertussis. This value was relatively high compared with other previous studies. Indeed, pertussis surveillance in French hospitals revealed that only 1% of B. parapertussis was isolated in infants presenting with symptoms of whooping cough over a period of 10 years.[18,19] In another study conducted in Tunisia whooping cough was attributed to B. parapertussis in 7% of cases.[18] In fact, studying pertussis infection in Pakistan from 2005-2009 unexpectedly identified 59 cases of B. parapertussis against only 5 cases of B. pertussis.[20] However, there is little understanding of the relationship between both species. B. pertussis can enhance B. parapertussis infection in mixed infection of the respiratory tract, through the action of pertussis toxin.[21] Prior antimicrobial treatment in 95.8% of clinically suspected patients with pertussis might also have resulted in failure attempts to recover bordetella species from clinical samples. As culture failure does not exclude a diagnosis of pertussis and using this procedure alone to diagnose whooping cough is likely to lead to underdiagnosis of this infection.[18] Although, 21 cases proved by culture had received antibiotic prior to taking culture their antibiotic might not be effective. This study indicates that 47.6% of confirmed cases were unvaccinated and 28.6% were partially vaccinated according to their age. These findings indicate a defect in vaccination coverage or lack of awareness of immunization importance. Similar result has been observed in Spain with 59.7% not being vaccinated.[10] In the present study, 58.3% of patients had positive family history of paroxysmal cough. Prolonged cough may be the only clinical feature in adolescent and adults who tend to seek medical advice for 2-3 weeks after the onset of symptoms or not at all. When they do present they are often misdiagnosed and may be a source of infection.[22] As reported by many studies, vaccination against pertussis does not result in lifelong immunity. Given this situation, immunization strategies are greatly needed to control pertussis in this age group as a means of decreasing transmission to young infants. It would be important to expand immunization to adults, focusing on those who are more likely to transmit infection to susceptible infants, including new parents, close contacts of newborns, health care workers and child care workers.[18] Leukocytosis (15000-100000 cells/mm3) due to absolute lymphocytosis is characteristic in the catarrhal stage.[23] In our study despite the mean leukocyte count was more than 15000 cells/mm3 in those children who had been proved to have pertussis or parapertussis but there was no significant difference when compared with others. This might be attributed to the fact that almost all of the patients received antibiotic or the blood sample were collected during the paroxysmal phase, although when we compare granulocyte count between micro-organisms that obtained by culture results were significant. Mean platelet count in this study was within normal range and this was in contrast to what is observed in a study done in Madrid were high platelet count were common finding in cases with clinical diagnosis of whooping cough.[24]

Conclusion

Improper vaccination status (partially or not vaccinated) was found in nearly half of patients included in this study. Gender, age and certain clinical and laboratory findings had no significant relation except for platelet count.

Conflicts of interest

The authors report no conflicts of interest.

References

1. Leber A, Salamon D, Prince H. Clinical microbiology newsletter 2011; 33 (15):111-5.
2. Howidi M, Nair R, Rajah J. The severity of pertussis in young infant in the United Arab

Emirates Proceedings of the ESPID. Annual Conference. Brussels, Belgium 2009; June 9-13
3. Burr S, Jenkins T, Harrison R, Meert K, Anand K, Berger J, et al. The Collaborative Pediatric Critical Care Research Network (CPCCRN) Critical Pertussis Study: Collaborative Research in Pediatric Critical Care Medicine. Pediatr Crit Care Med 2011; 12(4):387-92.
4. Communicable disease toolkit, Iraq crisis. WHO, March 2003, available from: http:// www.who.int/diseasecontrol_emergencies/toolkits/ Iraq_profile_ok.pdf (accessed on 17 of january 2013)
5. Al-Bargish K A. Outbreak of pertussis in Basra, Iraq. East Mediterr Health J 1999; 5(3):540-8.
6. Colorado Department of Public Health and Environment (homepage on internet) Summary of Pertussis Investigation and Control Guidelines [cited 2011 June 11, accessed at 17 of January 2013]. Available from: http://www.colorado.gov/cs/Satellite/CDPHE-Main/ CBON/1251583470000
7. Crespo I, Cardenosa N, Godoy P, Carmona G, Sala M., Barrabeig I, et al. Epidemiology of pertussis in a country with high vaccination coverage. Vaccine 2011; 29(25):4244-8.
8. Al-Shammary M. The descriptive epidemiology of pertussis in Al Diwaniya governorate for the years 1990 through 2007, Kufa Med Journal 2010;13(2): 7-17.
9. Cardenosa N, Romero M, Quesada M, Oviedo M, Carmona G, Codina G, et al. Is the vaccination coverage established enough to control pertussis, or it is a re-emerging disease? Vaccine 2009; 27 (25-26):3489-91.
10. Ferrer A, Moraga F, Olsina M, Campins M, Planells I. Culture-confirmed whooping cough in a tertiary center over a twelve-year period. An Pediatr (Barc) 2003; 58(4):309-15.
11. Muhsim M, Al-Tufaili Y,Shalan A. The epidemiological profiles of hospitalized pertussis patients in Babylon province. Kufa Med Journal 2009; 12(2):230-9.
12. Al-Tawfiq J, Abukhamsin A. Bordetella pertussis infection in highly vaccinated population in Saudi Arabia, 1996-2004. J infection 2007; 55(3):249-53.
13. Mughal A, Kazi Y, Bukhari H, Ali M. Pertussis resurgence among vaccinated children in Khairpur, Sindh, Pakistan. Public Health 2012; 126 (6):518-22.
14. Yildirim I, Ceyhan M, Kalayci O, Cengiz A, Secmeer G, Gur D, et al. Frequency of pertussis in children with prolongued cough. Scand J Infect Dis 2008; 40(4):314-9.
15. Baptista P, Magalhães V, Rodrigues L.Children with pertussis inform the investigation of other pertussis cases among contacts. BMC Pediatr 2007; 7:21.
16. Hochwald O, Bamberger ES, Rubin L, Gershtein R, Srugo I. A pertussis outbreak among daycare children in Northern Israel: who gets sick? Isr Med Assoc J 2010; 12(5):283-6.
17. Cengiz A, Yildirim I, Ceyhan M, Seçmeer G, Gür D, Kara A. Comparison of nasopharyngeal culture, polymerase chain reaction (PCR) and serological test for diagnosis of pertussis. Turk J Pediatr 2009; 51(4):309-16.
18. Zouari A, Smaoui H, Brun D, Njamkepo E, Sghaier S, Zouari E, et al. Prevalence of Bordetella pertussis and Bordetella parapertussis infections in Tunisian hospitalized infants: results of a 4 year prospective study. Diagn Microbiol Infect Dis 2012; 72(4):303-17.
19. Bonmarin I, Levy-Bruhl D, Baron S, Guizo N, Njamkepo E, Caro V, et al. Pertussis surveillance in French hospitals: results from a 10 year period. Euro Surveill 2007; 12(1):34-8.
20. Bokhari H, Said F, Syed M, Mughal A, Kaziy F, Heuvelman K, et al. Whooping cough in Pakistan. Bordetella pertussis vs Bordetella parapertussis in 2005-2009. Scand J Infect Dis 2011; 43:818-20.
21. Worthington Z, Van Roooijen N, Carbonetti N. Enhancement of Bordetella parapertussis infection by Bordetella pertussis in mixed infection of the respiratory tract. FEMS Immunol Med Microbiol 2011; 63:119-28.
22. Mattoo S, Cherry JD. Molecular pathogenesis, epidemiology, and clinical manifestations of respiratory infections due to Bordetella pertussis and other Bordetella subspecies. Clin Microbiol Rev 2005; 18:326-82.
23. Long S, Kleigman R, Stanton B, Geme J, Schor N, Behrman R. Pertussis. Nelson textbook of pediatrics.19th edition. Philadelphia: Elsevier Saunders; 2011. p 945.
24. Francis M, Borque C, del Castillo F, Díez J, García J. Whooping cough: a retrospective study of the cases diagnosed over a period of 15 years. An Esp Pediatr 1998; 49(3):280-3.