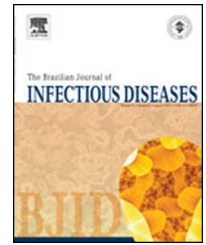




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Original article

Pertussis may be the cause of prolonged cough in adolescents and adults in the interepidemic period



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ABSTRACT

Objective: This study was aimed to evaluate the prevalence of pertussis in adolescents and adults with cough lasting more than 14 days and less than 30 days.

Methods: This is a prospective observational study in interepidemic period of pertussis. Ten public health outpatient clinics in the city of Recife, Brazil, were randomly selected for the study. The study population consisted of individuals aged 10 years and over with cough that had lasted between 14 and 30 days. Nasopharyngeal swabs were collected for culture and PCR in order to identify *Bordetella pertussis*. We adopted the Centers for Disease Control and Prevention in the US (CDC) definition of cases of pertussis.

Results: A total of 192 individuals were identified as suspected cases. Their mean age was 40.7 years. Pertussis was confirmed in 10 of the 192 suspected cases, with an estimated prevalence of 5.21% (95% confidence interval 2.03–8.38). All cases met the clinical case definition for pertussis; one suspect had both culture and PCR positive. PCR confirmed 100% of the cases, 7/10 by PCR and 3/10 by epidemiological linkage with a case confirmed by PCR.

Conclusion: During an interepidemic period, 1 in 20 cases of prolonged cough had pertussis, suggesting this is an important cause of prolonged cough in adolescents and adults.

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Introduction

Epidemics of pertussis, an increase in of the number of pertussis cases in adolescents, adults and infants younger than six months of age have been reported in several regions of the world.¹⁻³ Adolescents and adults have often been identified as the main source of pertussis outbreaks amongst household members.⁴⁻⁶ The World Health Organization estimates that there were around 16 million cases of pertussis and 195,000 deaths worldwide, 95% of which were in developing countries.²

The clinical presentation of pertussis in adolescents and adults is often atypical, with a prolonged, persistent, nonspecific cough and in these age groups the diagnosis of pertussis is seldom considered.⁷⁻⁹ Although many studies have reported that prolonged cough in adolescents and adults may be pertussis, the actual prevalence of pertussis in this age group remains underestimated.² In 2010, the Centers for Disease Control and Prevention in the US (CDC) registered 27,550 cases of pertussis in the US, and in Europe the European Center for the Control and Prevention of Diseases registered 15,749 cases, with a higher prevalence in adolescents between the ages of 10 and 14 years.^{10,11} In studies conducted in different regions of the world the prevalence of pertussis amongst adolescents and adults with prolonged cough has varied from 10% to 32%.^{9,12,13} The variety of diagnostic methods and case definitions used may be one of the major reasons for the differences in the observed prevalence.^{7,9,14,15} Nonetheless, these studies have contributed to strategies for controlling the surveillance of pertussis in these countries.^{2,10,11}

In Brazil, since the introduction of the pertussis vaccine in 1980, the number of reported cases fell sharply with a sustained downward trend. However in 2011, 583 cases of pertussis were confirmed. Amongst the confirmed cases, 76.3% were infants under 1 year of age, the group with highest incidence and mortality rates.¹⁶ In the city of Recife, most notifications of pertussis are hospitalized cases. A study carried out in Recife identified that adults and adolescents older than 11.5 years were the source of infections for 70% of pertussis cases.⁴ However, this study analyzed cases of pertussis in adult contacts of children with pertussis.¹⁷

This study is aimed to evaluate the prevalence of pertussis in adolescents and adults with cough lasting more than 14 days and less than 30 days.

Methods

This is a prospective observational study in interepidemic period of pertussis. The study was conducted in 10 public health outpatient clinics in the city of Recife, Brazil. The outpatient clinics from within the city's six Health Districts were randomly selected with proportional probability of the number of patients attended. Health professionals and individuals attending the health clinics were informed of the study. During the period from August 2010 to July 2011, those over the age of 10 years, with cough lasting more than 14 days and less than 30 days were identified. Nasopharyngeal swabs for culture and PCR were collected from all participants. Individuals who

were immunocompromised, suffered from TB, had chronic bronchitis, other chronic diseases with cough, or using drugs that cause coughing were excluded from the study. A suspected case of pertussis was considered as a confirmed case if the individual presented a cough and a positive nasopharyngeal swab culture, or met the clinical case definition criteria for pertussis and had a positive PCR. The criteria for defining a clinical case of pertussis were: a cough for more than 14 days, associated with at least one other symptom: paroxysmal cough, inspiratory whooping, post-tussive vomiting regardless of age and vaccination status. An epidemiologically confirmed case was considered when the individual met the clinical criteria of a pertussis case, had a negative culture and/or PCR, but was in contact with an individual with pertussis confirmed by culture or PCR. Material for the culture and PCR was collected by nasopharyngeal swab from individual nostrils for each procedure. The swabs for collecting the culture were inoculated in a transport medium of 50% of the Regan-Lowe concentration medium (Oxoid Ltd., Columbia, MD) for the culture and for the laboratory in a Reagan Lowe medium (Oxoid. Ltd., Columbia, MD), made selective by the addition of 40 mg/L cephalexin. The colonies suspected as being *B. pertussis* were confirmed by biochemical tests. The real-time PCR used primers and TaqMan[®] probes, specifically for the IS 481 region.^{14,18,19} The study was approved by the Ethics Committee at Hospital Oswaldo Cruz, registration number 029/2008. All participants signed the Terms of Free, Informed Consent. Data were coded and processed using Epi-info 6.0.4 (CDC). The descriptive analysis of the data was conducted by frequency distribution and the means with the respective standard deviations. In the comparative age analysis of the suspected cases, according to positivity for pertussis, the student t-test was applied to independent samples tested for normality by the Komogorov-Smirnov test. In the analysis of associations, when the independent variable was categorical, the Fisher's exact test was applied. The statistical significance adopted for the study was 5% ($p < 0.05$). A prevalence of 25% was assumed for calculating the sample size, an acceptable maximum error of 6% and a confidence interval of 95%. The estimated required sample was 201 patients. The study was conducted in 10 outpatient clinics from amongst the 12 randomly selected clinics. Two clinics were excluded since it was not possible to select patients due to operational difficulties. The patients identified at the excluded clinics were transferred to other clinics in the same district, which made part of the selected clinics and corresponded to 5.26% (10/192) of the selected sample total.

Results

A total of 192 individuals were identified aged over 10 years and with cough lasting for more than 14 days. The mean age was 40.7 years, ranging from 10 to 84 years and a SD \pm 17.8 years. Of these, 55.7% (107/192) were over 40 years of age, 27.6% (53/192) were aged between 20 and 39 years and 16.7% (32/192) between 10 and 19 years. A total of 70.0% (134/192) of the suspected cases were female; 182/192 of the suspected cases were unable to inform their vaccination status. The

Table 1 – Criteria for confirming the diagnosis of pertussis in adolescents and adults with a prolonged cough.

	Positive for pertussis		
	Positive	(%)	95% CI
<i>Criteria for confirmation</i>			
Culture	1/10	10%	0.25–44.5%
Real-time PCR	7/10	70%	34.7–93.3%
Epidemiological linkage	3/10	30%	6.7–65.2%

remaining 10 individuals who reported having received the 4-dose DPT vaccine were aged between 10 and 19 years. Of the 10 confirmed pertussis cases, the vaccination status was reported by three individuals, two confirmed that they had received four doses of DPT, and one confirmed three doses. Of these, one was diagnosed with pertussis by culture and PCR, and the others, by PCR. Of the 192 suspected pertussis cases, 171/192 (89%) reported cough of between 14 and 21 days and 21/192 (11%) for more than 21 days. Inspiratory whooping was reported by 120/192 (62.5%), cyanosis by 27/192 (14.1%) and post-tussive vomiting by 152/192 (79.1%). Amongst the 192 suspected cases, pertussis was confirmed in 10 individuals, thus estimating a prevalence of 5.21% (95% CI 2.03–8.38). The culture and PCR were positive for *B. pertussis* in one patient (Table 1) and all confirmed cases by PCR epidemiologically met the clinical criteria for defining a case of pertussis. The clinical characteristics and epidemiological descriptions of the 10 pertussis confirmed cases are in Table 2. Amongst the 10 confirmed cases of pertussis, five were primary cases, four were co-primary and one was secondary. Of these, five were index cases that led to the identification of five new cases.

Discussion

One in 20 cases of prolonged cough was found to have pertussis. This study was conducted during an interepidemic period.¹⁶ This fact may possibly have influenced the number of individuals eligible for the study and in estimating the prevalence of pertussis. The mean age of the individuals with a cough for more than 14 days was 40.7 years. Studies

undertaken in Canada, Denmark and France reported a mean age of between 41 and 49 years. In the present study, only 10 patients were able to inform whether they had taken DPT vaccine against pertussis. Of these, one was diagnosed with pertussis by culture and PCR and the others by PCR. As the participants of this study were aged over 10 years, the final dose of the vaccine for pertussis would have been applied at least 8 years previously. The pertussis vaccine was first introduced into the Brazilian vaccine program in 1983 and since 2003; vaccine coverage for three doses of the vaccine has remained above 95%.¹⁶ In around 90% of the suspected cases, the cough had lasted for a period of 14–21 days and 110 (57.29%) met the clinical criteria for pertussis. Gilberg et al., in France, during a period of low prevalence of pertussis, reported that 79% of confirmed cases met the clinical criteria. Strebel, in the US, observed that 85% of confirmed cases of pertussis met clinical criteria.¹² The high prevalence of cases that met clinical criteria may be explained by the fact that those with more severe symptoms were more likely to seek medical care. This in turn, could explain why the prevalence of pertussis in adolescents and adults who present cough as the only symptom is underestimated. Culture only confirmed the diagnosis in just one of the ten patients with pertussis (10%). PCR confirmed 100% of the cases. Several studies have demonstrated low culture sensitivity for confirming a case of pertussis as compared to PCR and blood tests.^{14,16,19} The patients included in the present study had cough for more than 14 days. It is believed that the timing of culture collection and the technical difficulties involved in conducting the test contributed to the low sensitivity of the study. The present study estimated a prevalence of pertussis of 5.21% in adolescents and adults with cough for more than 14 days. Studies conducted in Australia, Canada, Denmark, France and the US reported prevalence ranging from 10% to 32%.^{8,9,11} As this study was carried out during an interepidemic period, did not use serology to confirm the diagnosis, and that the material for the culture and PCR was collected between 14 and 30 days after the onset of cough, may have underestimated the prevalence of pertussis resulting in a lower prevalence than that in other countries. The high prevalence found is relevant because adults and adolescents are the main source of infection for infants under 1 year of age, the age when pertussis has the higher rate of complications and death.^{1,3,5-7}

Table 2 – Clinical and epidemiological characteristics of adolescents and adults with a prolonged cough and diagnosed with pertussis.

Cases	1	2	3	4	5	6	7	8	9	10
Sex	F	F	F	M	M	F	F	M	F	M
Age (years)	28	14	20	43	43	45	15	29	34	24
Days with cough	18	14	15	20	14	14	14	15	14	18
Paroxysm	+	+	+	+	+	+	+	+	+	+
Whoop	–	+	+	+	+	+	+	+	+	+
Cyanosis	–	–	–	–	–	–	+	+	–	–
Apnea	+	–	–	–	–	–	+	+	+	+
Post-tussive vomiting	+	+	+	+	+	–	–	–	–	–
Vaccination ^a	3	1	2	3	3	3	1	3	3	3

F: female; M: male.

^a Vaccination: 1 – complete vaccination (4 doses DTP); 2 – incomplete vaccination (minor than 3 doses DTP); 3 – unknown.

Conclusion

Even in an interepidemic period, pertussis was shown to cause one in 20 cases of prolonged cough in adolescents and adults.

Recommendation

Pertussis is underdiagnosed among adolescents and adults. Health professionals should be more aware and have high index of suspicion to recognize pertussis as cause of cough illness, even in the absence of local outbreak. The implementation of adolescents and adults immunization could protect the infants.

Conflicts of interest

The authors declare no conflicts of interest.

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