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ORIGINAL ARTICLE

Clinical, laboratorial and radiological aspects of patients admited with suspected pertussis

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Abstract

Objective: Describe the profile of patients admitted with signs of pertussis, emphasizing the differences between confirmed cases and its differential diagnosis. **Methods:** Retrospective study realized by the analysis of medical charts of patients from 0 to 2 years old, admitted between 2015 to 2019 with suspected pertussis. Epidemiological, clinical, laboratorial, and radiological variables were verified. The data was analyzed descriptively and through associations. **Results:** 211 patients were included, being 81,1% levss than 6 months old and 49,3% male. At the admission, high frequency of coughing (99.1%), paroxysmal coughing (60,2%), cyanosis (78,7%) and dyspnea (70,1%) was observed. Data showed that 8,4% of the patients who underwent leukogram presented lymphocytic leukocytosis, and 57,5% of the patients submitted to chest X-ray presented abnormalities. The pertussis diagnosis was confirmed in only 37 patients. There was significative association (p<0,005) between pertussis and the variables: cyanosis, post-cough vomiting, inspiratory squeak, tachypnea, respiratory auscultation abnormalities and leukocytosis. Furthermore, 72,9% of the patients did not get the vaccine or the schedule was incomplete. **Conclusions:** The presentation of pertussis, in general, is similar to other respiratory infections, being fundamental the maintenance of the epidemiological surveillance to collaborate with the diagnosis, reduce use of macrolides and adequate the prophylactic measures.

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INTRODUCTION

Acute respiratory infection is a public health concern in the pediatric age group, especially in developing countries.[1] Diagnosis may be challenging, since the signs and symptoms produced by the infectious agents causing these diseases are quite similar.[2]

In this context, whooping cough is an acute respiratory disease caused by Bordetella pertussis, known to cause significant infant morbidity and mortality. In Brazil, epidemiology studies have described a gradual decrease in the incidence of whooping cough since the 1990s due to the expansion of vaccination coverage. However, a sudden increase in the number of cases has been observed since 2011, with incidence peaking in 2014. Despite the decrease in the number of cases observed between 2014 and 2019, the Ministry of Health recommended the strengthening of epidemiological surveillance programs in order to monitor the trends around the incidence of disease to allow the early detection of cases and the implementation of relevant efforts to control it.[3,4]

The symptoms of whooping cough include paroxysmal dry cough, potentially accompanied by cyanosis, apnea, vomiting and inspiratory gasp.[4] These manifestations tend to occur more severely in neonates and infants, in whom respiratory viral infections are common and a relevant item to consider in differential diagnosis. Pathogens mimicking whooping cough often manifest symptoms such as wheezing, bronchiolitis and pneumonia. Therefore, patients suspected for whooping cough must undergo confirmatory diagnostic testing so that adequate care is provided.[5,6]

Despite the similarities between the symptoms of whooping cough and other acute respiratory infections, patients management differs, especially with regard to the use of macrolides and in-hospital prevention.[7] Therefore, knowing the main characteristics of suspected patients, as well as the differences between confirmed cases and other conditions listed in differential diagnosis, is fundamental for clinical characterization, timely diagnosis and the adoption of appropriate treatment and preventive approaches to the disease. This study describes the epidemiological, clinical, workup and imaging profile of newborns and infants hospitalized for whooping cough and lists the traits that distinguish Bordetella pertussis infection from other acute respiratory infections.

METHOD

This cross-sectional descriptive analytical study was carried out at a referral hospital for maternal and child health in Pernambuco. Patients aged up to two years admitted between 2015 and 2019 suspected of having whooping cough were included. Confirmatory cultures were performed. Records with missing pages or records with illegible content were excluded. The hospital's Epidemiology Office aided in enrollment by making the records of patients with diagnostic tests performed.

Data collection was carried out between the months of May and August 2021 based on the medical records available in the medical archive, organized into standardized forms. Epidemiological variables included year of hospitalization, age, sex and vaccination history. The typical signs and symptoms of whooping cough and other conditions included in differential diagnosis were considered, such as presence or absence of cough, paroxysmal cough, cyanosis, post-cough vomiting, inspiratory gasp, fever, nasal obstruction, dyspnea, tachypnea, grunting, facial plethora, prolonged expiration and altered lung sounds. Workup tests included leukogram at admission, C-reactive protein, blood culture and culture for Bordetella pertussis. Presence or absence of alterations in chest X-rays were considered and the diagnosis produced at the time of discharge was recorded. The vaccination status of the patients diagnosed with whooping cough was checked for the pentavalent (diphtheria, tetanus, pertussis, hepatitis B, and Haemophilus influenzae type b) and the DPT vaccine; mothers were also checked for diphtheria, tetanus, and acellular pertussis (DTaP) vaccination during pregnancy.

The collected data were included in an Excel spreadsheet and statistical analysis was performed on IBM SPSS 25.0. Descriptive results were obtained based on absolute and relative frequencies for categorical variables and measures of central tendency and dispersion for numerical variables. The Pearson Chi-Square test and Fisher's Exact Test were used to evaluate the association between two categorical variables. Standard error in the statistical tests was set at 5% and a 95% confidence interval was defined.

The study was approved by the institution's Human Research Ethics Committee (certificate no. 35992620.3.0000.5201). The study complied with the requirements set out in Resolution 466/12 of the National Council of Health.

RESULTS

Twenty-three of the 234 patients initially included in the study were excluded. The mean age of the 211 study participants was 4.11 months (± 4.65) and the median age was 3.00 months. Twenty-five (11.9%) were aged less than one month; 146 (69.2%) were aged between one and six months; 26 (12.3%) were aged between seven and 12 months; and 14 (6.6%) were aged between 13 and 24 months. One hundred and four (49.3%) were males and 107 (50.7%) were females. An increase in the frequency of suspected and confirmed cases of whooping cough per year was observed, as seen in Table 1.

Cough was the most commonly described symptom of pertussis, observed in 209 (99.1%) patients, with 127 (60.2%) reports of paroxysmal cough. Cyanosis was described in 166 (78.7%) patients, post-cough vomiting in 67 (31.8%) and inspiratory gasp in 26 (12.3%) patients. Regarding other signs and symptoms seen in acute respiratory infections, 148 (70.1%) patients had dyspnea, 100 (47.4%) had altered lung sounds in

Table 1. Number of suspected and confirmed cases of whooping cough admitted to a maternal and child health referral center between 2015

Variable	n (%)
Number of suspected cases of whooping cough per year	
2015	9 (4.3)
2016	27 (12.8)
2017	26 (12.3)
2018	46 (21.8)
2019	103 (48.8)
Total	**211 (100.0)**
Number of confirmed cases of whooping cough per year[1]	
2015	1 (2.7)
2016	5 (13.5)
2017	1 (2.7)
2018	9 (24.3)
2019	21 (56.8)
Total	**37 (100.0)**

(1) Percentages calculated based on the 37 patients with positive cultures for *Bordetella pertussis*.

respiratory auscultation, 93 (44.1%) had fever, 49 (23.2%) had tachypnea, 32 (15.2%) had nasal obstruction, 20 (9.5%) had prolonged expiration, 10 (4.7%) had facial plethora and five (2.4%) had grunting recorded as a symptom.

In terms of lab tests, we found that 178 (84.4%) patients had leukograms. Table 2 shows the measures of central tendency and dispersion for leukogram results. Fifteen (8.4%) patients had lymphocytic leukocytosis and ten (5.6%) had neutrophilic leukocytosis. Forty-eight (24.2%) patients (22.7%) had levels of C-reactive protein measured, and 17 (35.4%) presented high CRP levels. Fifty-one patients had blood cultures done, and 37 (72.5%) had a negative result recorded in their records. Finally, regarding culture Bordetella pertussis, 174 patients (82.5%) had negative results and 37 (17.5%) had positive results.

Chest X-rays were performed in 163 (77.3%) patients, the results of which were described in the medical records of 120 (73.6%) patients, with one or more alterations identified in 69 (57.5%) cases. The following findings were recorded: 41 (59.4%) cases of pulmonary infiltrates; 12 (17.4%) of pulmonary condensation; six (8.7%) of lung opacity; two (2.9%) of atelectasis; four (5.8%) of increased cardiac area; and 21 (30.4%) of straightened costal arches.

Diagnoses of whooping cough based on cultures were seen in only 37 (17.5%) patients. At discharge, 105 (49.8%) patients were diagnosed with pertussis syndrome, 24 (11.4%) with acute viral bronchiolitis, 19 (9.0%) with community-acquired pneumonia and 20 (9.5%) with nonspecific respiratory tract infection.

An association was evinced between neonates and infants with a diagnosis of whooping cough and clinical, laboratory and imaging findings. Considering signs and symptoms at admission, a significant association was observed between whooping cough and cyanosis ($p = 0.031$), post-cough vomiting ($p = 0.015$), inspiratory gasp ($p = 0.025$), tachypnea ($p = 0.049$) and altered lung sounds ($p = 0.045$), as shown in Table 3. Interestingly, the proportion of patients with cyanosis diagnosed with whooping cough was greater than the proportion of individuals not diagnosed with this condition (91.9% vs. 75.9%); the proportion of patients with post-cough vomiting was greater among individuals with Bordetella pertussis infection than in patients without infection (48.6% vs. 28.2%); the proportion of patients with inspiratory gasp was greater among individuals with whooping cough than in individuals with other conditions (24.3% vs. 9.8%); the proportion of patients with tachypnea was greater among individuals not diagnosed with whooping cough (25.9% vs. 10.8%); the proportion of patients with altered lung sounds was higher among individuals with other respiratory tract infections compared to patients with whooping cough (50.6% vs. 32.4%).

In workup tests, there was a significant association between confirmed cases of whooping cough and leukocytosis ($p = 0.007$), as seen in Table 4. The proportion of patients with leukocytosis was greater in individuals with Bordetella pertussis infection than in subjects without infection (81.8% vs. 34.8%). X-ray alterations were not significantly associated with a diagnosis of whooping cough.

Regarding the vaccination status of patients diagnosed with whooping cough, we found that 10 (27.0%) had not been vaccinated, 17 (45.9%) had incomplete vaccination cards and 10 (27.0%) were not asked about it. The vaccination of mothers during pregnancy was not described in 34 (91.9%) cases.

DISCUSSION

The analysis of the epidemiological profile of the included patients revealed that 81.1% were aged six months

Table 2. Measures of central tendency and dispersion of leukogram results in patients with suspected pertussis admitted to a pediatric hospital

Variable	Mean ± SD	Median
Total leukocytes	28048.00 ± 17002.21	21700.00 (19650.00; 27400.00)

Table 3. Association between signs and symptoms at admission and diagnosis of whooping cough.

Variable	Whooping cough			
	Yes n (%)	No n (%)	Group totals n (%)	p-value
Inspiratory gasp				p (2) = 0.025*
Yes	9 (24.3)	17 (9.8)	26 (12.3)	
No	28 (75.7)	157 (90.2)	185 (87.7)	
Post-cough vomiting				p (1) = 0.015*
Yes	18 (48.6)	49 (28.2)	67 (31.8)	
No	19 (51.4)	125 (71.8)	144 (68.2)	
Cyanosis				p (1) = 0.031*
Yes	34 (91.9)	132 (75.9)	166 (78.7)	
No	3 (8.1)	42 (24.1)	45 (21.3)	
Tachypnea				p (1) = 0.049*
Yes	4 (10.8)	45 (25.9)	49 (23.2)	
No	33 (89.2)	129 (74.1)	162 (76.8)	
Altered lung sounds				p (1) = 0.045*
Yes	12 (32.4)	88 (50.6)	100 (47.4)	
No	25 (67.6)	86 (49.4)	111 (52.6)	
Total	**37 (100.0)**	**174 (100.0)**	**211 (100.0)**	

(*) Significant association at 5%.
(1) Based on Pearson's Chi-square test.
(2) Based on Fisher's Exact test.

Table 4. Association between leukogram results at admission and diagnosis of whooping cough.

Variable	Whooping cough			
	Yes n (%)	No n (%)	Group totals n (%)	p-value
Leukocytosis				p (1) = 0.007*
Yes	9 (81.8)	16 (34.8)	25 (43.9)	
Não	2 (18.2)	30 (65.2)	32 (56.1)	
Total	**11 (100.0)**	**46 (100.0)**	**57 (100.0)**	

(*) Significant association at 5%
(1) Based on Fisher's Exact test.

or less, as also seen in a similar cross-sectional study enrolling 80 inpatients with suspected whooping cough, in which 81.2% were aged up to 6 months.[8] Considering patients aged one year or less, we found that 93.4% were admitted with suspected whooping cough, as expected given the high incidence of the disease in this age group.[9] No significant difference was observed between genders, as outlined in previous epidemiological studies.[10,11]

A significant annual increase in the number of patients with suspected and confirmed diagnoses of whooping cough was observed. This is possibly due to the fact that the study was carried out in Pernambuco, a state in Northeastern Brazil in which there was an increase of more than 20% in the number of suspected and confirmed cases of Bordetella pertussis infection between 2018 and 2019, although the incidence of the disease is on a downward trend nationwide.[3]

There is a scarcity of references in the literature about the purely descriptive results that cover the signs and symptoms at admission of patients with suspected whooping cough against which our article might be compared. Current

literature describes the challenges in achieving a diagnosis of acute respiratory tract infection derived from the fact that different pathogens produce similar signs and symptoms on patients with disease.[2] As the 211 patients included on our study were analyzed for the presence of typical signs and typical symptoms, we found that 209 presented with cough, 127 with paroxysmal cough, 166 with cyanosis and 67 with post-cough vomiting, all of which have been described as the most prevalent symptoms of the disease.[4] Nonetheless, only 37 participants had a positive culture for Bordetella pertussis, a fact that corroborates the non-specificity of clinical manifestations.

Regarding laboratory tests, leukograms can be used to help confirm or rule out suspected cases. The presence of leukocytosis and lymphocytosis has been linked with strong clinical suspicion of disease. Although indicated by the Ministry of Health for the investigation of pertussis, absence of changes in a leukogram does not rule out the presence of disease.[4] In our study, only 8.4% of the patients with a leukogram had leukocytosis due to increased lymphocyte counts. We also found that 22.7% of hospitalized patients had CRP levels measured and 24.2% had blood cultures performed. However, we should also note that there is no formal indication for carrying out these tests in patients with suspected Bordetella pertussis infection; these tests were performed on account of other diagnostic hypotheses, in order to mitigate unnecessary testing and achieve greater benefits to patients and public health.[4,12]

In regard to imaging, the Ministry of Health recommends that chest X-ray images be acquired for patients under four years of age with suspected whooping cough, in order to aid in diagnosis and detect complications.[4] Despite the indication, approximately 20% of the patients included in our study did not have chest X-ray images done, possibly due to the lack of knowledge of healthcare workers about this recommendation. Nonetheless, alterations were found in 57.5% of the patient with chest X-ray images, with pulmonary infiltrate and straightening of costal arches as the most frequent findings. Few studies have described X-ray alterations in patients with suspected whooping cough, which is also an element that distinguishes our study from others. Nonetheless, literature about chest X-ray alterations in patients with acute respiratory infection cites pulmonary infiltrate, straightening of costal arches and consolidations as the more common anomalies, as also seen in our study.[13]

Only 17.5% of patients had culture tests confirming a diagnosis of whooping cough. The main diseases included in differential diagnosis were acute viral bronchiolitis and community-acquired pneumonia, both caused by agents related to pertussis syndrome. In this context, in a study carried out with patients hospitalized for acute respiratory illness, a similar proportion (24.7%) of patients had a laboratory diagnosis of whooping cough, although confirmation was achieved with PCR tests only. A study including patients with suspected bronchiolitis found that Bordetella pertussis infection in 8.5% of the cases, which reaffirms the possible similarity between the two conditions.[6,14,15]

It is important to mention that this study found significant associations between diagnosis of whooping cough and clinical and workup findings. The most common signs of disease in patients with Bordetella pertussis infection were cyanosis ($p = 0.031$), post-cough vomiting ($p = 0.015$) and inspiratory gasp ($p = 0.025$) when compared to patients with other infections. In this regard, a study carried out with children hospitalized for acute respiratory infection demonstrated that cyanosis was a more common finding in individuals diagnosed with whooping cough compared to individuals diagnosed with acute viral bronchiolitis ($p < 0.006$ and $p < 0.005$, respectively).[16] Our results were also reported in a similar study carried out in 2013, which demonstrated positive predictive values above 80% connecting cyanosis and inspiratory gasp with a clinical diagnosis of whooping cough.[5]

Our study found a significant association between presence of whooping cough and leukocytosis ($p = 0.007$). Another study about respiratory infections in patients with suspected whooping cough also found that significant leukocytosis was useful in differentiating between confirmed cases of whooping cough and other respiratory tract infections. Evidence indicates that leukocytosis above 20,000/mm^3 increases the chance of a diagnosis of whooping cough.[5,6] Although no significant associations were found between chest X-ray alterations and whooping cough of pertussis in our study, current literature indicates that pulmonary infiltrate is the most common alteration, as seen in the X-ray images of patients with suspected whooping cough.[17]

Most of the medical records of patients with whooping cough included in our study did not contain information on vaccination coverage, as also reported in other epidemiological studies.[9,18] Medical records should be filled up thoroughly in order to allow proper analysis of quality of care.[19] Nevertheless, based on the data available in medical records, we found that 27.0% of the patients had not been vaccinated, and 45.9% had an incomplete immunization status. Another study with 1,209 patients with whooping cough revealed that 32.2% of the patients were not vaccinated and 44.1% had an incomplete immunization status.[9]

According to the Ministry of Health, individuals gain immunity against whooping cough with three doses of the pentavalent vaccine and two booster shots of the DTP vaccine, with vaccination starting from four years of age.[20] Evidence indicates that the majority of the cases of whooping cough are seen in individuals with an incomplete immunization status.[3,9] However, our study cannot be used to confirm this statement, since only newborns and infants were included.

The description of hospitalized newborns and infants with suspected Bordetella pertussis infection and the associations between symptoms and a diagnosis of whooping cough found in our study indicate the existence of similarities

between the signs and symptoms of whooping cough and other acute respiratory infections. The impact of the disease on child morbidity and mortality points out to the need to perform epidemiological surveillance and disseminate evidence about the main characteristics of patients with suspected whooping cough and the specificities of differential diagnosis, in order to increase the number of cases confirmed with cultures and improve molecular and bacterial resistance tests, as recommended by the Ministry of Health. Furthermore, testing clearly expedites diagnosis, minimizes the widespread use of macrolides and allows the prompt adjustment of preventive measures.

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