Clinical-epidemiological study of Bordetella pertussis infection in the Gran Canaria island in the period, 2008–2016

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Abstract
Objective: Describe the epidemiological and clinical pattern of Bordetella pertussis infection (whooping cough) among hospitalised infants less than one year-old in a paediatric hospital in Gran Canaria.

Patients and methods: A retrospective review of the patient hospital records was performed, and recording only those with a microbiological diagnosis of pertussis infection detected using polymerase chain reaction, from January 2008 to December 2016.

Results: A total of 110 patients were identified, of which 105 (95.4%) were less than 6 months old, and 59.1% were males. The annual incidence of hospital admissions was estimated between 13.7 and 425.0 cases per 100,000 infants <12 months old, with 2 peaks in 2011 and 2015. Household members were the main potential sources of infection. Main clinical features were pertussis cough associated with signs of catarrh, cyanosis, and lymphocytosis. Complications occurred in 15.4% of the patients (mainly pneumonia), but the outcome was favourable in all the cases. A lower age and non-vaccination were associated with an increased risk of developing complications (p < .05). Viral co-infection occurred in 31.6% of infants diagnosed with pertussis.


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Introduction

Pertussis is a vaccine-preventable infectious disease caused by *Bordetella pertussis*. In recent years, there has been evidence of an increased incidence in many countries with a high vaccination coverage. Variations in published incidence rates may be due to differences in case reporting systems and access to diagnostic tests, but the highest rates are always reported in infants aged less than 1 year, who also experience the most complications and highest mortality. The Canary Islands is one of the autonomous communities in Spain with the highest rates of infection. In the 2003–2007 period, we performed a study where we found a high incidence of complications and mortality in this age group. For this reason, since 2015, vaccination of pregnant women was introduced in our autonomous community. In order to determine the subsequent trends of infection, we have conducted a clinical-epidemiological study of all the cases diagnosed in infants aged less than 1 year that visited the emergency department of the only public paediatric hospital in the island of Gran Canaria between 2008 and 2016.

Patients and methods

Patients

The study included the 1,040 patients aged less than 1 year that visited the emergency department of the Hospital Materno Infantil de Gran Canaria (which serves an average of 6,770 infants aged less than 1 year) with a clinical presentation that required ruling out *B. pertussis* between January 2008 and December 2016.

Methods

All patients underwent testing for detection of *B. pertussis* by means of polymerase chain reaction (PCR) (LightMix Kit Bordetella pertussis/parapertussis or Diagenode Bordetella pertussis/parapertussis) in samples of nasopharyngeal exudate obtained with a flexible swab. Viral detection tests were also performed 581 patients (55.9%) in nasopharyngeal aspirate samples.
We performed a retrospective review of the health records of patients who tested positive for *B. pertussis*, collecting data on demographic variables, vaccination history, probably source of infection (contacts with clinical features compatible with pertussis), symptoms, laboratory data and treatment.

In the statistical analysis, we used the Mann–Whitney U test to compare quantitative variables and the chi square test to compare proportions. We defined statistical significance as a p-value of less than .05. The study was approved by the local bioethics and research committee.

**Results**

**Epidemiology**

Infection by *B. pertussis* was detected in 110 patients (10.6%). A different pathogen was identified in 269 patients (25.7%): respiratory syncytial virus in 175, rhinovirus in 33, parainfluenzavirus 3 in 32, metapneumovirus in 7, cytomegalovirus in 5, influenza A in 5, influenza B in 4, enterovirus in 3, parainfluenzavirus 1 in 2, parainfluenzavirus 2 in 2, and coxsackievirus B in 1.

Of the 110 infants with infection by *B. pertussis*, 65 were male (59.1%). The mean age was 83.3 days (range, 14–287 days), and 105 (95.4%) were aged less than 6 months. Eleven had been born preterm (10.0%).

Fig. 1 shows the annual incidence of pertussis cases per 100,000 infants aged less than 1 year that sought care in the hospital. The annual incidence ranged between 13.7 cases in 2009 and 425.0 cases in 2015, with 2 peaks in years 2011 and 2015. Since 2010, the year with the lowest incidence was 2016. When it came to the seasonal distribution, 33.6% of cases occurred in summer, 29.1% in spring, 19.1% in winter and 18.2% in autumn.

As for the vaccination status of the patients, 56 infants (50.9%) had not started to receive routine vaccinations, 47 (42.7%) had received 1 dose, 5 (4.5%) 2 doses and 2 (1.8%) 3 doses. Only 1 child was incorrectly vaccinated for age.

A probable source of infection was documented in 45 patients (40.9%), corresponding to household members in 44 cases (97.8%) and nosocomial infection in 1.

Seventeen infants with pertussis were born after the introduction of vaccination of pregnant women; in 5 of these infants (29.4%) the mother had received the vaccine in the third trimester of pregnancy (one at 28 weeks, one at 31 weeks, timing not documented in the remaining 3). The mean age of these 5 infants was 2.8 months (range, 0–5 months).

**Clinical manifestations**

Table 1 presents the clinical manifestations and abnormal laboratory findings in 110 patients. The characteristic clinical presentation consisted of whooping cough accompanied by cold symptoms, cyanosis and lymphocytosis. The only difference in clinical characteristics between older infants and infants aged less than 3 months was the development of pneumonia, which only occurred in those aged less than 3 months (p < .01). The mean time elapsed from onset of symptoms to the emergency department visit was 9.0 ± 5.9 days (range, 1–28 days). A total of 107 patients were admitted to hospital (97.3%) for a mean length of stay of 10.7 ± 7.3 days (range, 0–45 days).

Complications developed in 17 patients (15.4%): 10 cases of pneumonia and 7 of apnoea. Table 2 presents the characteristics of the infants that developed complications: 82.3% had not started vaccination, and the rest had only received 1 dose. Nine infants with pneumonia were admitted to the intensive care unit (ICU). One girl aged 42 days (case 1) that was admitted to the ICU had originally presented with a leucocyte count of 27,200 cells/µL, but at 13 days from onset had developed hyperleukocytosis (103,000 leucocytes/µL), so she underwent a double volume exchange transfusion. Table 3 shows the differences between infants that developed complications and infants that did not. Their comparison reveals that infants who developed complications were younger and that a higher proportion of patients in this group had not initiated routine vaccinations.

All patients received treatment from the time of admission with azithromycin (10 mg/kg/day) for 5 days (except 1 patient treated for 10 days), with favourable outcomes.

**Coinfection with other pathogens**

Fifty-seven patients (51.8%) with infection *B. pertussis* underwent viral detection tests, which revealed in 18 (31.6%): by rhinovirus in 9, parainfluenzavirus 3 in 3, respiratory syncytial virus in 2, adenovirus in 1, influenza C in 1, cytomegalovirus in 1 and coxsackievirus B in 1.

**Discussion**

Despite the high vaccination coverage in the paediatric population, pertussis continues to be a significant health problem that recently led to the introduction of vaccination of pregnant women in the autonomous community of the Canary Islands with the intent to protect infants, the most vulnerable subset. Pertussis is a disease that causes epidemics on a cyclical pattern, although since 2010 in Spain there has been a sustained epidemic, which was reflected in our study. This phenomenon coincides with the re-emergence of pertussis observed both in the United States and in other European countries due to reasons that are yet unknown; some of the reasons that have been
Furthermore, according to the research, this significant decrease in attack rates, especially in infants aged less than 3 months, as described in previous studies,\textsuperscript{17} but we found no other differences in other signs and symptoms between the 2 age groups.

The population aged less than 1 year is at higher risk of complications. We observed complications in 15.4% of patients, mostly pneumonia. Younger age and unvaccinated status were the most significant factors associated to the development of complications, although none of the patients died. Compared to the preceding period, we found a lower rate of complications (23.4% in the 2003–2007 period) and a lower mortality (6.5% in the 2003–2007 period). Other studies have found a higher rate of complications in this age group.\textsuperscript{17} Several studies have analysed different variables and have found a higher risk of death or more severe disease in infants aged less than 4 months with low birth weight, hyperleukocytosis (≥100 000 leukocytes/μL), who develop pulmonary hypertension or seizures or with unvaccinated status, among others.\textsuperscript{18–20} and a high degree of suspicion in these patients would probably improve clinical outcomes.

Viruses were detected in a high proportion of patients in whom \textit{B. pertussis} infection was ruled out. The virus detected most frequently was respiratory syncytial virus, which demonstrates the overlap of signs and symptoms in this subset of the population, a fact that has been described by other authors.\textsuperscript{21,22} Furthermore, a viral coinfection was detected in a small proportion of the sample (most commonly by rhinoviruses), which was consistent with previous studies in which rhinoviruses and coronaviruses were most frequently detected in cases of coinfection.\textsuperscript{23}

In conclusion, in recent years there has been an increase in the incidence of pertussis in infants aged less than 1 year in our region associated with decreases in the incidence of complications and in mortality compared to the previous period. Younger age and unvaccinated status

\begin{table}[h]
\centering
\begin{tabular}{|l|c|c|c|}
\hline
\textbf{Clinical manifestations} & \textbf{Age ≤ 3 months (%)} & \textbf{Age >3 months (%)} & \textbf{Total (%)} \\
\hline
Cough & 65 (100) & 44 (97.8) & 109 (99.1) \\
Whooping cough & 56 (86.2) & 32 (71.1) & 88 (80.0) \\
Cold symptoms\textsuperscript{a} & 43 (66.2) & 30 (66.7) & 73 (66.4) \\
Cyanosis & 35 (53.8) & 22 (48.9) & 57 (51.8) \\
Posttussive vomiting & 20 (30.8) & 12 (26.7) & 32 (29.1) \\
Fever & 8 (12.3) & 8 (17.8) & 16 (14.5) \\
Apnoea & 7 (10.8) & 2 (4.4) & 9 (8.2) \\
Pneumonia & 10 (15.4) & 0 (0) & 10 (9.1) \\
Tachypnoea & 3 (4.6) & 0 (0) & 3 (2.7) \\
Polypnoea & 2 (3.1) & 0 (0) & 2 (1.8) \\
\hline
Laboratory findings\textsuperscript{b} & n = 64 & n = 43 & n = 107 \\
Lymphocytosis: absolute (≥10 000/mm\textsuperscript{3}) or relative & 58 (90.6) & 41 (95.3) & 99 (92.5) \\
Leucocytosis (≥17 500/mm\textsuperscript{3}) & 30 (46.9) & 15 (34.9) & 45 (42.1) \\
Thrombocytosis (≥450 000/mm\textsuperscript{3}) & 43 (67.2) & 24 (55.8) & 67 (62.6) \\
\hline
\end{tabular}
\caption{Clinical manifestations and laboratory findings in the 110 patients with infection by \textit{B. pertussis}.}
\begin{flushleft}
\textsuperscript{a} Upper respiratory tract disease: rhinorrhoea, coryza, sneezing or lacrimation.
\textsuperscript{b} Data from 107 patients (97.3%).
\end{flushleft}
\end{table}
Table 2  Characteristics of patients that developed complications.

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (days)/sex</th>
<th>Vaccination</th>
<th>Leucocytes per $\times 1000/mm^3$</th>
<th>Coinfection</th>
<th>Complications</th>
<th>ICU admission</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>42/F</td>
<td>No</td>
<td>103.0</td>
<td>–</td>
<td>Pneumonia, hyperleukocytosis</td>
<td>Yes</td>
<td>AZM 5 days, MV, sedation/muscle relaxation, exchange transfusion, inhaled adrenaline, dexamethasone iv</td>
</tr>
<tr>
<td>2</td>
<td>17/M</td>
<td>No</td>
<td>18.1</td>
<td>–</td>
<td>Pneumonia</td>
<td>Yes</td>
<td>AZM 5 days, MV, sedation/muscle relaxation, PN</td>
</tr>
<tr>
<td>3</td>
<td>24/M</td>
<td>No</td>
<td>32.0</td>
<td>–</td>
<td>Pneumonia, ischaemic necrosis of RLE requiring amputation</td>
<td>Yes</td>
<td>AZM 5 days, MV, sedation/muscle relaxation, PN</td>
</tr>
<tr>
<td>4</td>
<td>33/M</td>
<td>No</td>
<td>16.7</td>
<td>–</td>
<td>Pneumonia</td>
<td>Yes</td>
<td>AZM 5 days, MV, sedation/muscle relaxation, PN</td>
</tr>
<tr>
<td>5</td>
<td>53/F</td>
<td>No</td>
<td>46.3</td>
<td>–</td>
<td>Pneumonia</td>
<td>Yes</td>
<td>MV, sedation/muscle relaxation</td>
</tr>
<tr>
<td>6</td>
<td>54/M</td>
<td>No</td>
<td>37.5</td>
<td>–</td>
<td>Pneumonia</td>
<td>Yes</td>
<td>AZM 5 days, MV, sedation/muscle relaxation, PN</td>
</tr>
<tr>
<td>7</td>
<td>65/M</td>
<td>1 dose</td>
<td>54.7</td>
<td>–</td>
<td>Pneumonia</td>
<td>Yes</td>
<td>AZM 5 days, MV, sedation/muscle relaxation, PN</td>
</tr>
<tr>
<td>8</td>
<td>46/F</td>
<td>No</td>
<td>50.0</td>
<td>RSV</td>
<td>Pneumonia, convulsive seizures</td>
<td>Yes</td>
<td>AZM 5 days, clonazepam</td>
</tr>
<tr>
<td>9</td>
<td>47/F</td>
<td>No</td>
<td>67.1</td>
<td>–</td>
<td>Pneumonia</td>
<td>Yes</td>
<td>AZM 10 days, oxygen, PN, enoxaparin, Inhaled adrenaline</td>
</tr>
<tr>
<td>10</td>
<td>72/F</td>
<td>No</td>
<td>No data</td>
<td>–</td>
<td>Pneumonia</td>
<td>No</td>
<td>AZM 5 days</td>
</tr>
<tr>
<td>11</td>
<td>27/M</td>
<td>No</td>
<td>7.3</td>
<td>Coxsackievirus B</td>
<td>Apnoea secondary to coughing fits</td>
<td>No</td>
<td>AZM 5 days, upright position and oxygen during fits</td>
</tr>
<tr>
<td>12</td>
<td>28/F</td>
<td>No</td>
<td>10.3</td>
<td>–</td>
<td>Apnoea secondary to coughing fits</td>
<td>No</td>
<td>AZM 5 days, upright position and oxygen during fits</td>
</tr>
<tr>
<td>13</td>
<td>41/M</td>
<td>No</td>
<td>10.2</td>
<td>Rhinovirus</td>
<td>Apnoea secondary to coughing fits</td>
<td>No</td>
<td>AZM 5 days, upright position and oxygen during fits</td>
</tr>
<tr>
<td>14</td>
<td>42/F</td>
<td>No</td>
<td>32.7</td>
<td>–</td>
<td>Apnoea secondary to coughing fits</td>
<td>No</td>
<td>AZM 5 days, upright position and oxygen during fits</td>
</tr>
<tr>
<td>15</td>
<td>69/M</td>
<td>No</td>
<td>11.5</td>
<td>–</td>
<td>Apnoea secondary to coughing fits</td>
<td>No</td>
<td>AZM 5 days, upright position and oxygen during fits</td>
</tr>
<tr>
<td>16</td>
<td>94/F</td>
<td>1 dose</td>
<td>21.0</td>
<td>–</td>
<td>Apnoea secondary to coughing fits</td>
<td>No</td>
<td>AZM 5 days, upright position and oxygen during fits</td>
</tr>
<tr>
<td>17</td>
<td>140/M</td>
<td>1 dose</td>
<td>10.1</td>
<td>–</td>
<td>Apnoea (1 episode before admission)</td>
<td>No</td>
<td>AZM 5 days, upright position and oxygen during fits</td>
</tr>
</tbody>
</table>

AZM, azithromycin; F, female; IV, intravenous; M, male; MV, mechanical ventilation; PN, parenteral nutrition; RLE, right lower extremity; RSV, respiratory syncytial virus.

*a* Peak leucocyte count during monitoring.
were the main risk factors associated with the development of complications. The incidence of pertussis and its complications would probably decrease with vaccination of pregnant women, so it is important that long-term followup studies be conducted to assess the effectiveness of this preventive measure.

Conflicts of interest

The authors have no conflicts of interest to declare.

References