

Seroprevalence of *Bordetella pertussis* in Healthcare Workers in a Portuguese Hospital

Mónica Cró Braz¹, Maria Helena Neves¹, Maria Favila Menezes², Ana Cristina Lopes², Maria José de Sousa², Ana Serrão Neto¹

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Abstract

Introduction: *Bordetella pertussis* causes an acute respiratory infectious disease that, in newborns and infants, can present with severe clinical manifestations or even death. In Portugal, whole cell *pertussis* vaccine introduced in 1965 was replaced, in 2006, by the acellular form. An increasing number of cases has been observed, with an incidence of 5.5 per 100,000 cases in 2016. The duration of protection against *pertussis* is unknown after the last immunization or disease itself. Healthcare staff working with children can be the source of infection of hospital outbreaks and, therefore, knowing the seroprevalence of *pertussis* among them can help to decide the potential need for vaccination in susceptible professionals.

Methods: Prospective study including healthcare workers from neonatology and paediatric departments as well as the clinical pathology laboratory of a Portuguese hospital. People with acute respiratory symptoms, pregnant or vaccinated against *pertussis* in 2016 were excluded. The seroprevalence for pertussis was tested through immunoglobulin G for pertussis toxin by enzyme-linked immunosorbent assay.

Results: The population tested was negative for immunoglobulin G *pertussis* toxin in 97.8% (88/90); only the remaining 2.2% (2/90) showed equivocal results.

Discussion: This population is potentially susceptible to *pertussis* infection and could be a reservoir for disease and for its transmission. A booster immunisation could be recommended to these individuals.

Keywords: *Bordetella pertussis*; Immunisation; Personnel, Hospital; Portugal; Sero-epidemiological Studies

Introduction

Bordetella pertussis infection is an acute infectious respiratory disease which may present a severe clinical

course and have a fatal outcome in newborns and small infants. Its worldwide prevalence in 2014 was around 24 million cases, and it caused 160,700 deaths in children under 5 years old.^{1,2}

In Portugal, the combined vaccine against diphtheria, tetanus and whole-cell pertussis (DTwP) was introduced in 1965 and, in 2006, it was replaced by the acellular component vaccine (DTaP). The Portuguese vaccination coverage against pertussis is over 95% at 12 months and at 7 years of life. However, a re-emergence of the disease has been reported in Portugal with an incidence of 5.5/100,000 in 2016 (2.2/100,000 in 2012).^{3,4}

The worldwide increased prevalence of the disease may be justified by several factors, among which the mutation and genetic evolution of the agent or the transition from a whole-cell pertussis vaccine to an acellular pertussis vaccine, since the latter, according to some studies, seems to offer less protection.⁵⁻⁸ The improvement of diagnosis with new methods for the detection of *Bordetella pertussis* (molecular techniques such as polymerase chain reaction) is also noteworthy.^{5,8}

Although it is a disease of compulsory notification, pertussis is an underdiagnosed disease, especially in older children, adolescents and adults who seem to be the main reservoirs. The duration of protection against the disease is unknown, although it is estimated to be between four and 12 years after the last administration of the vaccine, and between four and 20 years after natural immunisation.³⁻⁸

The vaccination of pregnant women against pertussis, between 20 and 36 weeks of gestation, was shown to be effective in the protection of newborns and small infants, and it was included in the national vaccination programme in 2017.⁴ However, other strategies to decrease the disease are needed. Healthcare professionals, especially those working in a paediatric department, may be responsible for hospital outbreaks, as shown in previous studies and, therefore, it is essential to know their immune status.⁹⁻¹⁰

This study aims to characterise the seroprevalence of

1. Child and Adolescent Centre, CUF Descobertas Hospital, Lisbon, Portugal

2. Germano de Sousa Laboratory Medicine Centre, CUF Descobertas Hospital, Lisbon, Portugal

Corresponding Author

Mónica Cró Braz

monica.c.braz@jmellosaude.pt

CUF Descobertas Hospital, Rua Mário Botas, 1998-018 Lisbon, Portugal

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Bordetella pertussis amongst healthcare professionals who work more closely with children, in the neonatology and paediatric departments and in the clinical pathology laboratory (CPL) of a Portuguese general hospital with basic, intermediate and differentiated care.

Methods

This prospective study included healthcare professionals who worked in January 2017 in the paediatric and neonatology departments and in the CPL of a Portuguese hospital equivalent to a regional hospital with basic, intermediate and differentiated care. The CPL professionals were included in the study as they work directly with the patients in the paediatric age. Physicians, nurses, nursing assistants, medical laboratory assistants and administrative assistants were included in the study. Pregnant women, participants with acute respiratory disease or to whom the pertussis vaccine was administered in 2016 were excluded from the study.

The following demographic data were collected:

- Age group: 18-24 years, 25-34 years, 35-44 years, ≥ 45 years;
- Gender: female, male;
- Occupational category: physician, nurse, nursing assistant, medical laboratory assistant, administrative assistant;
- Workplace: paediatric emergency department, neonatology inpatient department, paediatric inpatient department, paediatric outpatient department, CPL;
- Date of the last pertussis vaccine.

The seroprevalence of the disease was evaluated using the serum *Bordetella pertussis* immunoglobulin G (IgG) testing Euroimmun IgG, with the enzyme-linked immunosorbent assay (ELISA) method - a quantitative assay of IgG antibodies to *pertussis* toxin. Photometric measurement of the colour intensity at the 450 nm wave length. Sensitivity of 100%. Specificity of 95.5%. Reproducibility: mean intra-assay variation (CV 2.6%), inter-assay variation (CV 5.9%). The test was considered positive (> 100 IU/mL), negative (< 40 IU/mL) or equivocal (40-100 IU/mL). Equivocal results were repeated.

Results

The sample distribution by age group is shown in Table 1, with 38% (34/90) of the participants in the 35-44 years age group, and 80% (72/90) female. About one-third are nurses (27/90), followed by physicians (26/90), nursing assistants (21/90), medical laboratory assistants (8/90) and administrative assistants (8/90), as shown in Table 2. The same table shows the distribution by

department. Professionals in the emergency department correspond to the highest percentage – 34% (31/90) (Tables 1 and 2) – of study participants.

About 98% (88/90) of the tested sample was negative for IgG antibody to *pertussis* toxin, with two equivocal results (50, 60 IU/mL) from a female nurse (35-44 years, emergency department) and a female physician (≥ 45 years, neonatology department).

Approximately 17% (15/90) of the healthcare professionals (all in the age group ≥ 45 years) were not vaccinated against *Bordetella pertussis* or their vaccination status was unknown. Four participants had lost their personal health booklet. All the other participants (70/90) had received the last dose of DTwP 20 years ago or more, except for a male physician (25-34 years, emergency department) who had a DTaP vaccine boost in 2006 and was also negative for IgG antibody to *pertussis* toxin.

Discussion

The results of this study identified a population of healthcare professionals of departments that work with children who are potentially susceptible to infection by *Bordetella pertussis*, although 79% of the sample had been vaccinated in childhood. Two equivocal and double confirmed results for IgG to *pertussis* toxin were obtained in a female nurse (35-44 years, emergency department) and in a female physician (≥ 45 years, neonatology department). These results may be due to cross-reactivity with other circulating antibodies (test specificity of 95.5%) or due to some residual immunity to this infectious agent. It is noteworthy that, despite being a young population, with 72% (65/90) of participants under the age of 45 years, all vaccinated with DTwP vaccine boost but one, they did not have any detectable IgG antibodies to *pertussis* toxin. This study reveals seronegativity for IgG antibodies to *pertussis* toxin that is similar to a Finnish study, in which 98.7% of the sample was negative.¹¹ However, a multi-centre study on the seroprevalence of *Bordetella pertussis* in healthcare professionals who work with children in Spain showed that 69% did not have any IgG antibody to *pertussis* toxin.¹² Another study in Iran found a seron-

Table 1. Distribution of the demographic data by age group

Age group (years)	Total, n (%)
18-24	4 (4)
25-34	27 (30)
35-44	34 (38)
≥ 45	25 (28)
Total	90 (100)

Table 2. Demographic data by occupational category and workplace

Occupational category	Emergency department	Neonatology inpatient department	Outpatient department	Paediatric inpatient department	Clinical Pathology Laboratory	Total n (%)
Nurses	12	9	3	3	0	27 (30)
Physicians	9	5	3	7	2	26 (29)
Nursing assistants	9	6	4	1	1	21 (23)
Medical laboratory assistants	0	0	0	0	8	8 (9)
Administrative assistants	1	2	4	1	0	8 (9)
Total n (%)	31 (34.4)	22 (24.4)	14 (15.6)	12 (13.3)	11 (12.2)	90 (100)

egativity for IgG to *pertussis* toxin in 52.4% in medical students.¹³ Similar studies have revealed heterogeneous values of seropositivity.¹⁴⁻²⁰

The ELISA method used in this study for the detection of IgG antibodies to *pertussis* toxin is reliable and has 100% sensitivity and 95.5% specificity. Other *pertussis* antibodies, such as the filamentous haemagglutinin, pertactin and fimbria, have been used in immunogenicity studies (humoral response). The role of cellular immunity after vaccination against pertussis is currently known to be through type 1 and 2 T helper cells. It is also known that memory B cells persist after both vaccines. The seronegativity for IgG antibodies to *pertussis* toxin does not necessarily mean a lack of protection against this disease, as cellular immunity may be effective.²¹ However, many questions of humoral and cellular immunity in the pertussis vaccine and the disease itself remain unclear.²² Hospital outbreaks of *Bordetella pertussis* with its origin in patients, healthcare professionals or visitors have been described, reflecting the ease of transmission also at the hospital level. Considering the morbidity and mortality of pertussis in premature infants, full-term newborns and small infants, healthcare professionals vulnerable to the disease and its transmission may be vaccinated, particularly those who work directly with small infants.²³⁻²⁴

According to the World Health Organization, a dose of the DTaP vaccine is recommended to all healthcare professionals who have not received it as adults and who work directly with patients. The Centers for Disease Control and Prevention advises healthcare professionals, regardless of age, to receive a dose of DTaP as soon as possible, if they have not previously received it.²⁵

In some countries, such as Spain, a dose of the DTaP vaccine for healthcare professionals who work with premature infants (2004) was recommended. Later, in 2011, a dose for all healthcare professionals who work in the paediatric and obstetrics departments was initially suggested.²⁶ Other countries have adopted similar recommendations to achieve higher vaccination coverage

against *Bordetella pertussis* in healthcare professionals but, to date, Portugal does not have official guidelines on this topic. It was not possible in this study to draw conclusions about the length of immunoprotection of DTwP versus DTaP.

The lack of knowledge of the correlation between the levels of IgG to *pertussis* toxin and the degree of protection of the individual is a limitation of this study. However, this method was used in several similar studies with international publications in journals with a high impact factor.¹²⁻¹⁶ The immune response to the *pertussis* vaccine and the disease itself is a challenge and, therefore, more immunogenicity studies are needed for the clarification of the role of serology in pertussis or, even, for the creation of other more reliable markers.

According to the international recommendations and the results obtained in this study, despite being a single centre study, seronegativity in healthcare professionals to *Bordetella pertussis* strengthens the hypothesis of a recommendation of a vaccine booster dose for individuals who work with children. Further Portuguese and multicentre studies on the seroprevalence of *Bordetella pertussis* in healthcare professionals would be important to substantiate this recommendation.

This population is potentially susceptible to infection by *Bordetella pertussis* and may be a reservoir of the disease and its transmission. A vaccine boost may be considered in these individuals.

WHAT THIS STUDY ADDS

- This is the first Portuguese study on the seroprevalence of *Bordetella pertussis* in healthcare professionals.
- It reinforces the need for more studies to understand the immunological memory conferred by the vaccine and the disease itself.
- It brings into discussion the possible need of a DTaP vaccine boost in healthcare professionals who work with children, as proposed by international recommendations.

Conflicts of Interest

The authors declare that there were no conflicts of interest in conducting this work.

Funding Sources

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Protection of human and animal subjects

The authors declare that the procedures followed were in ac-

cordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data

The authors declare that they have followed the protocols of their work centre on the publication of patient data.

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Seroprevalência de *Bordetella pertussis* em Profissionais de Saúde num Hospital Português

Resumo:

Introdução: A infeção por *Bordetella pertussis* é uma doença respiratória infecciosa aguda que, em recém-nascidos e pequenos lactentes, pode apresentar-se com um quadro clínico grave e mesmo morte. Em Portugal, a vacina contra a difteria, tétano e tosse convulsa de célula inteira foi introduzida em 1965, substituída, em 2006, pela vacina acelular. Nos últimos anos tem-se observado um aumento do número de casos, com uma incidência de 5,5/100 000 em 2016. Desconhece-se o tempo de proteção após vacinação ou imunização natural. Os profissionais de saúde podem ser causadores de surtos hospitalares em unidades pediátricas pelo que o conhecimento da seroprevalência de *Bordetella pertussis* poderá determinar a eventual necessidade de vacinação destes indivíduos.

Métodos: Estudo prospetivo incluindo profissionais de saúde dos departamentos de pediatria, neonatologia e laboratório de patologia clínica de um hospital português. Indivíduos

com doença respiratória aguda, grávidas e vacinados com pertussis no ano de 2016 foram excluídos. A seroprevalência da doença foi testada através da imunoglobulina G de toxina pertussis pelo método ELISA.

Resultados: Da população testada, 97.8% (88/90) foi negativa para anticorpo imunoglobulina G pertussis; os restantes 2.2% (2/90) mostraram resultados equívocos.

Discussão: Esta população encontra-se potencialmente suscetível à infeção por *Bordetella pertussis*, podendo constituir um reservatório de doença. Um reforço vacinal poderá ser recomendado a todos os indivíduos.

Palavras-Chave: *Bordetella pertussis*; Coqueluche; Estudos Soroepidemiológicos; Hospitais Pediátricos; Infeção Hospitalar; Portugal; Recursos Humanos em Hospital; Portugal; Transmissão de Doença Infecciosa