



## Seroprevalence of pertussis among healthcare workers: A cross-sectional study from Tunisia



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### ABSTRACT

This cross-sectional study aimed to assess pertussis seroprevalence among healthy healthcare workers (HCW) of the Children's Hospital of Tunis, Tunisia. During the study period, 236 blood samples were obtained to determine HCW exposure to pertussis. Concentrations of immunoglobulin G (IgG) to pertussis toxin (PT) were measured using a commercial enzyme-linked immunosorbent assay. Cut-offs values used were 40 and 100 IU/ml, respectively indicative of an infection within the last year and a current/recent infection. Overall, seropositivity rate was 11.4% (95% CI 7.4–15.5) and 2.5% (95% CI 0.5–4.6) of ELISA results were indicative of a current infection. Seroprevalence was significantly most important in nurses ( $p = 0.03$ ) and in participants aged 21–31y ( $p = 0.009$ ). Our study confirmed that pertussis is circulating in hospital settings and affecting Tunisian HCW, in close contact with infants. Therefore, a booster dose of acellular pertussis vaccine needs to be considered.

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### 1. Introduction

Pertussis, a preventable infectious disease caused by *Bordetella pertussis*, remains a public health concern in many countries despite high vaccination coverage rates [1]. Infants and young children are mostly affected [1]. Even if a decrease in mortality and morbidity is observed worldwide, the disease remains endemic all around the world [1]. Therefore, many countries have introduced various pertussis vaccination strategies for adolescents, but also adults and healthcare workers (HCW) in close contact with children, in order to prevent pertussis in the most vulnerable infants and reduce individual morbidity [2–4].

Nosocomial pertussis outbreaks involving infants, whose primary source of infection was HCW with unsuspected pertussis, have been well-described [2,5,6]. Indeed, HCW could contribute in the transmission of pertussis to their patients and the generation of severe cases among hospitalized infants too young to have completed their primary vaccination [2,7].

The World Health Organization (WHO) recommended a single dose of Tetanus-Diphtheria-acellular Pertussis (Tdap) vaccine for HCW who are in direct contact with patients and who have not previously received it as an adult [8]. According to the Advisory

Committee on Immunization Practices (ACIP), vaccinating HCW with Tdap can boost antibody concentrations to the antigens in the vaccine, will protect them against pertussis and is likely to decrease transmission to patients, household members, other HCW, and persons in the community [9]. Therefore, ACIP also recommended a single dose of Tdap as soon as feasible if they have not previously received Tdap and regardless of the time since their most recent tetanus-diphtheria vaccination [9]. France recommends vaccination of HCW overall. Those who are in close and repeated contact with infants under 6 months are given priority [10]. Whereas Austria, Norway and Finland recommend pertussis vaccination for pediatricians and healthcare workers in neonatal departments [3].

Seroprevalence studies have been performed in many countries and have shown significant differences in pertussis incidence rates, likely due to different diagnosis methods, vaccination coverage rates and vaccine type [11]. It is generally considered that cut-offs of anti-PT IgG values of over 125 IU/ml or 100 IU/ml are indicative of recent infections during the last year. Whereas those over 50 IU/ml or 62.5 IU/ml are compatible with infections in the past few years [11]. However, few studies about pertussis seroprevalence in developing countries using wP, including Tunisia, are available.

In Tunisia, circulation of pertussis in hospitalized infants has been previously described [12], despite high vaccination coverage (95.9%) for primo-vaccination (DTP3) [13]. Pertussis surveillance and diagnosis have been implemented since 2007 using culture and/or

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real time Polymerase Chain Reaction (PCR). In a hospital-based prospective study including 599 hospitalized infants aged < 1 year with/without suspected pertussis, 20.0% of samples were positive for *Bordetella* spp. Greater prevalence (94.0%) was among young infants under 6 months [12]. According to the National Immunization Program (NIP), infants are immunized against pertussis at the age of 2, 3 and 6 months using whole cell vaccine (wP) (Pentavac®, Serum Institute of India). A booster dose is administered at the age of 18 months [14]. Pertussis boosters for adolescents, adults or HCW have not been introduced neither recommended in the NIP to date.

The main aim of our study was to assess the seroprevalence of immunoglobulin G (IgG) to pertussis toxin in healthy HCW at the Children's Hospital of Tunis, according to age category, gender and profession. This will determine their susceptibility to transmit the disease to vulnerable infants, for whom pertussis might be associated with severe complications.

## 2. Methods

This cross-sectional study was carried out between 20 February 2017 and 15 March 2018, at the Children's Hospital of Tunis, the only university pediatric hospital in Tunisia. Participants were randomly selected. Eligibility criteria included healthcare professionals who are potentially exposed to patients and/or infectious materials. Enrolled participants were from different professions: physicians, nurses, other clinical workers such as biologists, ancillary nurses, laboratory personnel and therapists and non-clinical workers. Socio-demographic variables were collected using a questionnaire and included: age, gender, profession and the hospital department the participant was working in (surgery, internal medicine, laboratory, etc). This study was approved by the Children's Hospital Ethics Committee and was conducted in accordance with the declaration of Helsinki. Participants had to provide written informed consent. All participants did not receive a booster dose of pertussis vaccine since the childhood as the vaccine, recommended for adults, is not provided in Tunisia.

Blood samples were obtained from enrolled participants and centrifuged, then sera were stored at  $-20^{\circ}\text{C}$  until analysis in the Laboratory of Microbiology, at the Children's Hospital of Tunis. Immunoglobulin G (IgG) antibodies to *B. pertussis* toxin (PT) concentrations were measured using commercial enzyme-linked immunosorbent assay (ELISA) (Euroimmun, Lübeck, Germany) according to the manufacturer's instructions and as previously described [15,16]. This assay has been validated by Riffelmann et al.; sensitivity and specificity were estimated to 91% and 90% respectively [15]. A participant was considered seronegative if the anti-PT IgG concentration was <40 IU/ml, seropositive if anti-PT IgG levels  $\geq 40$  IU/ml. Concentrations were classified as high using a cut-off of 100 IU/ml indicative of recent or current pertussis infection. IgG-PT levels between 40 IU/ml and 100 IU/ml were indicative of pertussis exposure in the last 12 months. Seropositive sera were confirmed by a second measurement of the concentration.

The prevalence of IgG antibodies was assessed according to gender, age groups (21–31 years; 32–41 years; 42–51 years and 52–61 years), hospital department (pediatric ward or non-pediatric ward) and professional level. Differences were calculated by the chi-square and Fisher's exact tests using the SPSS Software version 25 (SPSS Inc., Chicago, USA). All confidence intervals (CI) were at 95%.

## 3. Results

Between February 2017 and March 2018, 236 HCW working in the Children's Hospital of Tunis accepted to participate in our

**Table 1**

Pertussis seroprevalence and anti-PT IgG levels according to demographic characteristics.

Variable	Anti-PT IgG level (IU/ml)			Seropositive cases n/n (%)	p value
	Median	Mean	Max		
<i>Gender</i>					
Female	8	17	200	20/197 (10.2)	0.16
Male	11	27	200	7/39 (17.9)	
<i>Age groups</i>					
21–31 y	9	22	200	20/119 (16.8)	0.009
32–41 y	8	17	200	5/68 (7.5)	0.20
42–51 y	8	12	67	1/26 (3.8)	0.19
52–61 y	10	15	110	1/23 (4.3)	0.26

seroepidemiological study. Median age was 31 years (range: 21–61 y), and 83.1% were female. Demographic and professional characteristics of the study population are detailed in Table 1. Professions of enrolled participants included: 47 physicians, 103 nurses, 70 other clinical workers (such as anaesthetist, biologist, radiologist, physiotherapist and nutritionist) and 16 non-clinical workers.

Overall, 27 HCW were seropositive (11.4%; 95% CI 7.4–15.5) and mean age was 29.5 years. Among them, 6 (2.5%; 95% CI 0.5–4.6) had very high anti-PT IgG levels indicative of a current or recent pertussis infection, whereas 21 (8.9%; 95% CI 5.3–12.5) had ELISA results indicative of an infection occurring within the last 12 months. Distribution of anti-PT IgG concentrations according to age is shown in Fig. 1. The highest levels ( $\geq 40$  IU/ml) were observed among HCW aged 21 to 40 years (Fig. 1).

Table 1 shows mean and median antibody levels according to demographic variables. Pertussis seroprevalence was significantly most important in participants aged 21–31y ( $p = 0.009$ ). No differences have been observed according to gender and other age groups. Seroprevalence by professional characteristics is described in Table 2. Nurses have been significantly most exposed to pertussis ( $p = 0.03$ ). No difference was found according to the other professions and to hospital department where participants are working.

## 4. Discussion

The main objective of our study was to determine seroprevalence of anti-PT antibodies in a cohort of Tunisian HCW. A total of 27 (11.4%) participants were seropositive. The presence of anti-PT antibodies in adult population could be either due to previous immunization or previous infection, as described earlier [7,16,17]. In our study, none had received pertussis vaccine since childhood. Therefore, seropositivity is due to an earlier infection. Thus, seropositive HCW could have transmitted the disease to infants in pediatric wards, who are too young to be fully vaccinated, or to other hospitalized persons at risk. Our findings are of particular concern because pertussis in HCW has never been described in Tunisia before. Moreover, anti-PT IgG levels  $\geq 40$  IU/ml were more frequently registered among HCW of childbearing age (21–40 years) who are likely to infect their newborns.

The situation outside Tunisia is a bit different from what was reported above: Hashemi et al. reported a seropositivity rate of 47.6% in Iranian medical students, whereas Higa et al. found 43.8% of anti-PT antibodies in HCW of a hospital in Japan [7,18–20]. Differences in seropositivity rates towards pertussis between countries could result from the different vaccination strategies, but also to the various ELISA kits and antigen used. Therefore, the results of pertussis seroprevalence studies should be compared with great caution [11].

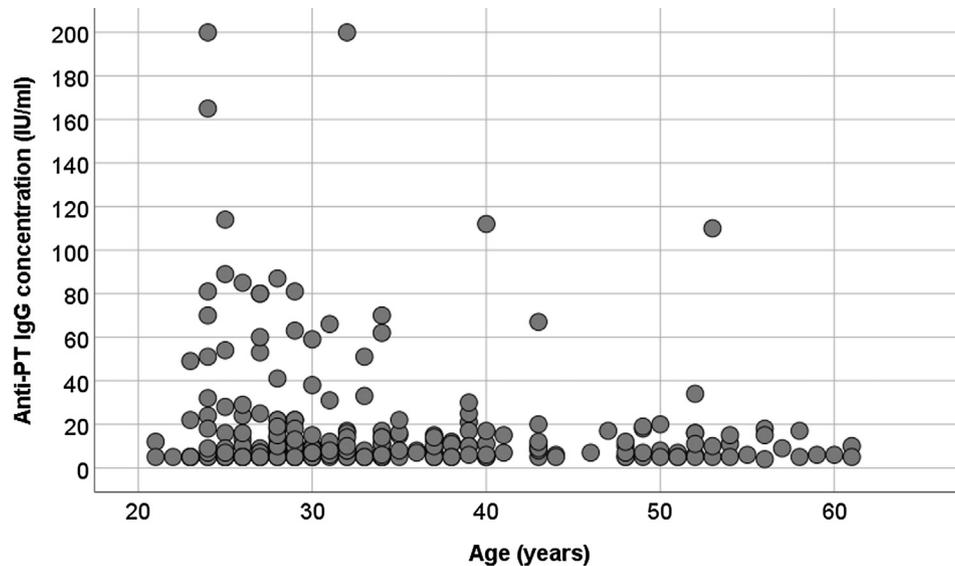


Fig. 1. Age-specific distribution of anti-PT IgG levels in enrolled participants.

Table 2

Pertussis seroprevalence and anti-PT IgG levels according to professional characteristics.

Variable	Anti-PT IgG level (IU/ml)			Seropositive cases n/n (%)	p value
	Median	Mean	Max		
<i>Professional level</i>					
Physician	8	16	87	5/47 (10.6)	0.8
Nurse	10	24	200	17/103 (16.5)	<b>0.03</b>
Other clinical workers	8	14	112	5/70 (7.1)	0.18
Non-clinical workers	5	9	31	0/16 (0)	0.14
<i>Hospital department</i>					
Paediatric ward (surgery, paediatrics)	9	20	200	25/191 (13.1)	0.1
Non-paediatric ward (laboratory ...)	8	16	200	2/45 (4.4)	

In our study, no significant differences in seroprevalence of anti-PT antibodies were found according to gender and hospital department, suggesting that exposure to pertussis could be generalized [21]. However, seroprevalence was significantly most important in nurses and participants aged 21–31y. Those are in childbearing age and could transmit the disease not only to hospitalized infants but also to their own babies. Different results have been observed elsewhere [7,18,22].

This seroepidemiological study highlights the importance of expanding vaccination against pertussis to HCW in close contact with infants. In fact, booster vaccination will protect them from work-related exposure to pertussis and prevent the spread of this illness that pose a threat to hospitalized new-borns and infants. Besides, nosocomial pertussis outbreaks, where HCW were the source of infections, have already been documented [9] and management of these outbreaks could be costly and disruptive to hospitals [6,9]. Therefore, HCW with increased newborn or infant contact, are a priority group in adult vaccination programs to reduce risk of transmission to infants. It has been confirmed that booster vaccination of pediatric HCW is likely to be cost-effective [6,9] and could prevent nosocomial pertussis outbreaks in neonatal intensive care units [3,5]. Nevertheless, if the baboon model is relevant to adult pertussis then aP may not prevent colonisation and transmission [23].

Various European countries have recommended pertussis booster vaccine, especially in pediatric and neonatal units, to avoid eventual further spread of the disease [2,3,24]. Moreover, vaccination of HCW in African countries is recommended by the Global

Pertussis Initiative [25]. However, in Tunisia, implementation is logistically difficult in absence of Tdap vaccine and the lack of updated adult immunization program. Therefore, reviewing pertussis immunization schedule in Tunisia is needed.

One limitation of this study was the low number of enrolled participants likely due to low recognition of adult pertussis disease. Also, the study was performed during a period of low pertussis incidence in Tunisia, in between two cycles. Otherwise, seropositivity rates would have been more important. However, our seroepidemiological study gave an idea of pertussis serological status at hospital level and may reflect the true situation in the other Tunisian hospitals, especially in pediatric and neonatal departments.

## 5. Conclusion

This study highlights the circulation of pertussis in Tunisian healthcare professionals in close contact with infants. Our findings suggest the necessity of introducing a booster dose of pertussis acellular vaccine (Tdap) in hospitals, especially for HCW working in pediatric and obstetric settings. Greater awareness among Tunisian HCW about the benefits of booster Tdap vaccination is required.

## Conflict of interest

None

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