

# Pediatric hospital healthcare workers and pertussis; a seroprevalence study

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## ABSTRACT

**Background.** This study aimed to assess pertussis seroprevalence among healthcare workers (HCWs) of a university children's hospital and to determine their opinions on whether to get the pertussis vaccine booster dose in adulthood.

**Methods.** This cross-sectional study was carried out between January 2018 and March 2019. Data recording forms were filled by the face to face interview method. Anti-pertussis toxin IgG (Anti-PT IgG) antibody levels were determined quantitatively from the serum samples using a commercial enzyme-linked immunosorbent assay (ELISA) kit. Anti-PT IgG results were interpreted according to World Health Organization (WHO) recommendations.

**Results.** Of the 169 HCWs included in the study, 67 (39.6%) were seronegative and susceptible to pertussis. Seropositivity was significantly higher among HCWs who worked 40–80 hours per week. Thirty-six (21.3%) HCWs had high anti-PT IgG levels, indicating recent infection in the past few years. High-level positivity was significantly more common among HCWs using macrolide antibiotics due to prolonged cough. Anti-PT IgG levels of three (1.8%) were compatible with acute infection and they were not followed up with suspicion of whooping cough and were not isolated. While 125 (74.0%) of the participants said they could get the pertussis vaccine booster dose, only three (1.8%) had done so.

**Conclusions.** The fact that 39.6% of HCWs were seronegative, emphasized the need for the pertussis booster dose. More than 20% of HCWs have had the acute infection without pertussis diagnosis in the past few years. Adult vaccination awareness in HCWs has not yet created a change in behavior. The high rate of seropositivity in macrolide users also shows that we cannot prevent its spread despite treatment. These findings highlight the fact that pertussis can occur in adult age groups and that eradication cannot be achieved without effective adult immunization and surveillance.

**Key words:** whooping cough, healthcare workers, seroprevalence, pertussis vaccine, attitudes.

Whooping cough is a highly contagious, vaccine-preventable disease that primarily affects infants. Primary pertussis vaccination programs have been implemented in most countries, and developed countries have high coverage rates for infants. Although the introduction of the pertussis vaccine dramatically reduced infection rates, it is known that neither infection nor immunization

produces lifelong immunity to pertussis.<sup>1</sup> Protective immunity wanes 4-12 years after the vaccination or 4–20 years after natural infection, resulting in re-infections in adolescents and adults.<sup>2</sup> As a result, numerous studies have documented an increased incidence of pertussis among adolescents and adults.<sup>3,4</sup> In a review from our country, it was mentioned that the frequency of whooping cough increases in adolescents and adults as in many countries.<sup>5</sup> The main concern is that these groups may be a source of infection for young infants who have not yet completed their primary immunization.<sup>6</sup> In particular, symptomatic or asymptomatic pertussis infections

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among healthcare workers (HCWs) pose a greater threat to public health than in other adults.<sup>7</sup> Most infected HCWs remain undiagnosed, and treatment and isolation are not always possible, thus endangering susceptible populations in hospitals such as newborns or preterm infants. Nosocomial pertussis outbreaks show that the number of infected individuals may increase and affect the entire population.<sup>8</sup> The Advisory Committee on Immunization Practices (ACIP) recommends that HCWs who have direct patient contact should receive a single dose of tetanus toxoid/diphtheria toxoid/acellular pertussis vaccine (adult formulation, Tdap) if they have not been vaccinated previously as an adult, regardless of when they received their last dose of tetanus toxoid/diphtheria toxoid (Td).<sup>9</sup> However, the World Health Organization (WHO) emphasizes that a decision to introduce adolescent and/or adult boosters should only be taken after careful assessment of local epidemiology.<sup>10</sup> For this reason, several pertussis seroprevalence studies have been conducted in Turkey.<sup>11-14</sup> However, to the best of our knowledge, none of these studies have investigated the pertussis seroprevalence among HCWs employed in pediatric hospitals in Turkey. Therefore, the aim of this study was to evaluate the pertussis seroprevalence of HCWs working in a university children's hospital.

## Material and Methods

This cross-sectional study was approved by the Clinical Research Ethics Committee of Dokuz Eylul University hospital (decision number 13.07.2017, 2017 / 18-40).

### Study population

The study included all nurses, resident physicians, and specialists aged 18 and over employed in the pediatric hospital of Dokuz Eylul University between January 2018 and March 2019 who agreed to participate. Written informed consent was obtained from all participants before the study. The data

registration form with questions about the participants' demographic characteristics, the units in which they worked, the patient profiles they worked with, and their immune status were completed in face-to-face interviews. The presence of cough persisting for longer than 3 weeks, the use of macrolide antibiotics due to prolonged cough, and vaccination history were evaluated based on the participants' verbal statements. They were also asked their opinions about the adult pertussis booster vaccination.

### Sample collection and antibody detection

Blood was collected from the study participants and the isolated serum samples were stored at - 20°C until analysis. Anti-pertussis toxin IgG (Anti-PT IgG) antibody levels were determined quantitatively from the serum samples using a commercial enzyme-linked immunosorbent assay (ELISA) kit (Cat No: EI 2050-9601 G, Brand: EUROIMMUN AG, Germany) as per the manufacturer's instructions. This kit has a lower limit of detection of 0.2 IU/ml, sensitivity of 95.5–97.8%, and specificity of 100%, and conforms to the latest serological diagnostic guidelines for *Bordetella pertussis* infections.<sup>15</sup>

Anti-PT IgG results were interpreted according to WHO recommendations. HCWs with anti-PT IgG level <10.0 IU/ml were considered seronegative, while those with ≥10 IU/ml were regarded as seropositive. The seropositive HCWs were further classified into three groups: Low-level positivity indicating no recent exposure (anti-PT IgG 10–40 IU/mL) and high-level positivity indicating recent infection in the past few years (anti-PT IgG ≥40 IU/mL) or current/very recent (last 12 months) infection (anti-PT IgG ≥100 IU/mL). None of the HCWs had been vaccinated in the past 2 years.

### Statistical analysis

Kolmogorov-Smirnov test was used to assess the normality of data distributions. Descriptive statistics were presented as mean and standard deviation, median and minimum–maximum values, and percentage distribution.

Comparisons of means between two groups were performed using Student's t test for normally distributed data and Mann-Whitney U test for non-normally distributed data. Means of more than two groups were compared using analysis of variance (ANOVA) for normally distributed data and Kruskal-Wallis test for non-normally distributed data. Chi-square analysis (Fisher's exact test when necessary) was used to compare the percentage distributions between the groups. Significance level was accepted as  $p < 0.05$ .

### Results

Of all HCWs employed in the children's hospital (n=198), 169 (85.4%) were included in the study. The mean age of the study group was  $30.4 \pm 5.9$  (23-52) years. Their demographic characteristics and occupational groups are presented in Table I.

The participants were divided into 3 groups according to hours worked per week: 50 (29.6%) worked  $\leq 40$  h/week, 88 (52.1%) worked 40-80 h/week, and 31 (18.3%) worked  $\geq 80$  h/week. Evaluation of these working hours by professional group is presented in Table II. All HCWs who worked  $\geq 80$  h/week were resident physicians and had been working in the children's hospital for 1 year or less (Table II).

Eighty-nine (52.7%) of the HCWs stated that they did not know their childhood pertussis vaccination status. While 125 (74.0%) of the participants said they could get the pertussis vaccine booster dose, only three (1.8%) had done so.

The mean anti-PT IgG antibody level of the entire study group was  $25.1 \pm 30.3$  IU/ml (5-200 IU/ml). Sixty-seven (39.6%) HCWs were evaluated as seronegative (anti-PT IgG  $< 10$  IU/ml), while a total of 102 (60.4%) HCWs were seropositive (anti-PT IgG  $\geq 10$  IU/ml) and were grouped according to their antibody levels (Fig. 1). Of the 136 female HCWs of childbearing age included in the study, 104 (76.5%) had anti-PT IgG levels below 30 IU/ml.

There were no significant differences in seropositivity based on gender ( $p=0.35$ ), age ( $p=0.21$ ), other demographic characteristics ( $p>0.05$ ), occupational group ( $p=0.72$ ), or the unit in which they worked ( $p=0.34$ ). Seropositivity was significantly higher among HCWs who worked 40-80 hours per week ( $p=0.03$ ). The distribution of seronegative and seropositive participants according to their working hours is shown in Figure 2.

Thirty-six (21.3%) HCWs had high anti-PT IgG levels ( $\geq 40$  IU/ml) indicative of recent infection in the past few years. There were no significant differences in high-level positivity based on gender ( $p=0.83$ ), age ( $p=0.65$ ), other demographic characteristics ( $p>0.05$ ), occupational group ( $p=0.31$ ), hospital department ( $p=0.68$ ), working hours ( $p=0.68$ ), or the presence of chronic cough in the past year ( $p=0.27$ ). However, high-level positivity was significantly more common

**Table I.** Characteristics of health care workers included in the study (n=169).

Characteristic	n (%)
Age group	
19-29 years	96 (56.8)
30-39 years	56 (33.1)
$\geq 40$ years	17 (10.1)
Sex	
Female	138 (81.7)
Male	31 (18.3)
Professional group	
Nurses	89 (52.7)
Resident physicians	56 (33.1)
Specialist physicians	24 (14.2)

**Table II.** Distribution of professional groups by hours worked per week.

Professional group	Hours worked per week		
	$\leq 40$ h n: 50 (29.6%)	40-80 h n: 88 (52.1%)	$\geq 80$ h n: 31 (18.3%)
Nurses	45 (90)	44 (50)	0 (0)
Resident physicians	2 (4)	23 (26.1)	31 (100)
Specialist physicians	3 (6)	21 (23.9)	0 (0)

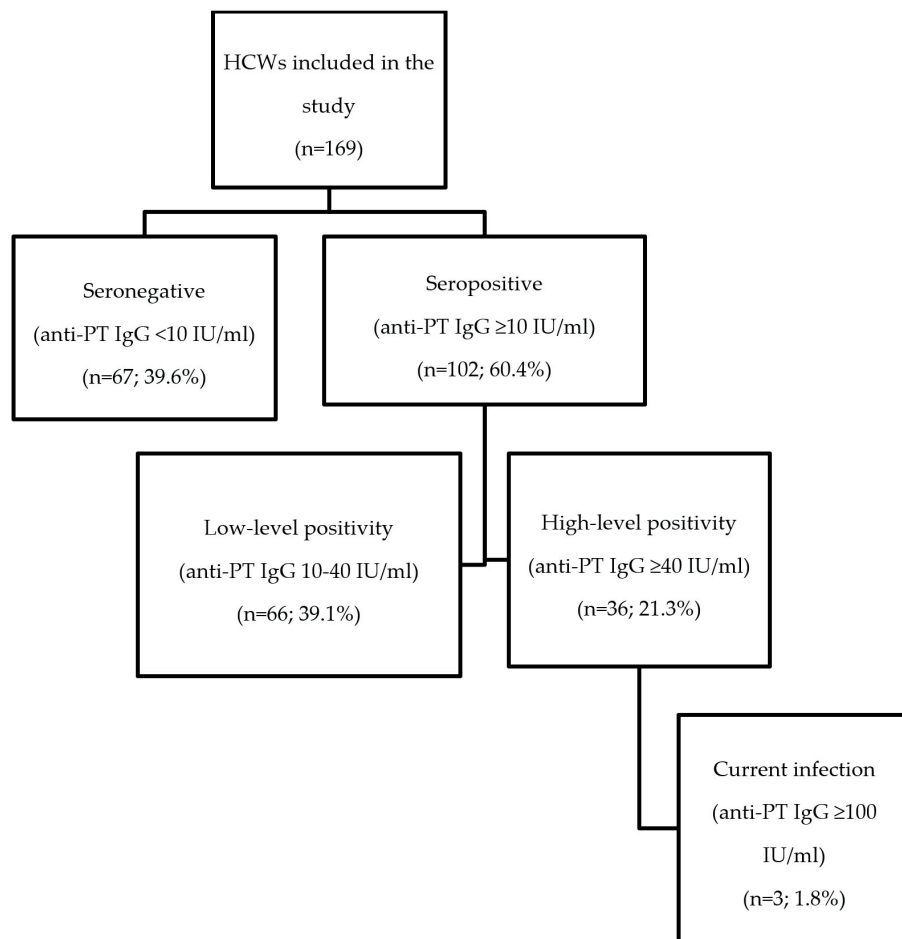


Fig. 1. Distribution of health care workers (HCWs) by anti-PT IgG level.

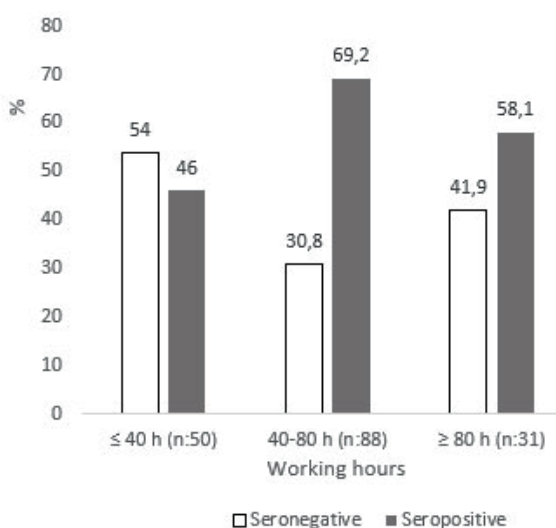


Fig. 2. Distribution of seronegative and seropositive health care workers (HCWs) according to hours worked per week.

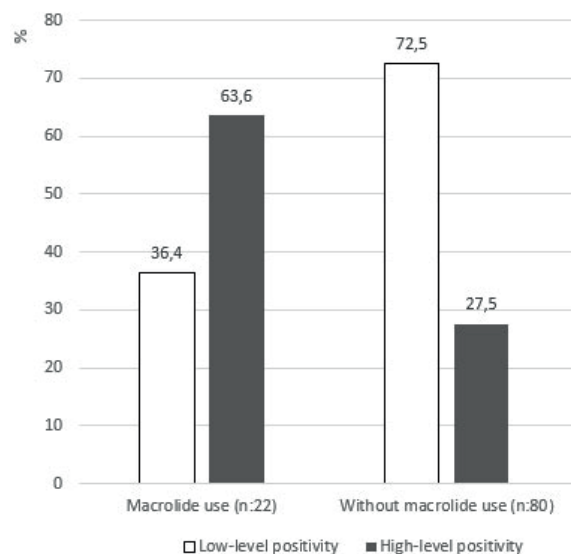


Fig. 3. Low-level and high-level seropositivity in health care workers with and without macrolide use due to persistent cough.

among HCWs using macrolide antibiotics due to prolonged cough than other HCWs ( $p=0.002$ ) (Fig. 3).

Three female HCWs of reproductive age had antibody levels above 100 IU/ml (115.7 IU/ml, >200 IU/ml, >200 IU/ml). None of them was tested or treated for suspected whooping cough and were not isolated. One of these HCWs was a specialist in the nephrology department, one was a nurse in the pediatric intensive care unit, and the other was a nurse in the neonatal intensive care unit. The antibody levels of the three HCWs who had received the booster dose were 55.5 IU/ml, 41.9 IU/ml, and 10.8 IU/ml. Of these participants, the two women HCWs stated that they were vaccinated during pregnancy and one male HCW received the vaccine while his wife was pregnant.

## Discussion

National vaccination programs in Turkey have included pertussis vaccines since 1937. Although 92% of children under the age of 5 were vaccinated in a mass vaccination campaign conducted in Turkey in 1985, 39.6% of the HCWs in our study were seronegative and susceptible (Fig. 1). Similarly, Urbiztondo et al.<sup>7</sup> found that 48.3% of HCWs in their study were susceptible, while Hashemi et al.<sup>16</sup> and Higa et al.<sup>17</sup> reported seronegativity rates of 52.4% and 56.2% among HCWs respectively. These data indicate that the susceptible population is increasing in other countries as well. It is known that the protective immune response provided by primary immunization with the acellular pertussis (aP) vaccine diminishes faster than with the whole cell (wP) vaccine and the duration of protection is 5–6 years.<sup>18</sup> Because the aP vaccine was introduced to Turkey in 2007, it is impossible for HCWs, nearly half of whom are susceptible, not to be affected by pertussis. As such, the development of a nosocomial pertussis epidemic is inevitable. Therefore, adult vaccination programs should be revised and pediatric HCWs should be considered a priority group to receive the pertussis vaccine booster dose.

Our results showed that 60.4% of HCWs in this study were seropositive. In a community-based seroprevalence study, Esen et al.<sup>11</sup> reported 60.8% seropositivity among 2,085 volunteers aged 0–60 years. In other studies from our country, pertussis seroprevalence rates between 8.5% and 90% were determined using different kits and thresholds in different age groups.<sup>11–14,19,20</sup> Only one study by Tanriover et al.<sup>14</sup> included HCWs, and even then they only represented 2.6% of the study group. Although no previous study conducted in Turkey focused exclusively on HCWs, pertussis seroprevalence among HCWs has been evaluated in many other countries, with results similar to ours.<sup>7,16,17,21,22</sup> Anti-PT antibody seropositivity in HCWs has been reported at rates of 51.7% by Urbiztondo et al.<sup>7</sup>, 43.8% by Higa et al.<sup>17</sup> among medical staff at a Japanese university hospital, and 47.6% among Iranian medical students in a study by Hashemi et al.<sup>16</sup> The reported prevalence varies between 10.2% and 98.7% in other studies conducted among HCW in different countries.<sup>7,16,17,21,29</sup> This wide range may be due in part to the use of different antigens and cut-off values, but may also reflect different epidemiological conditions.<sup>24</sup> Although anti-PT IgG levels were determined using the ELISA method in all of those studies, it is difficult to compare their results due to the absence of an FDA-approved ELISA kit.<sup>8</sup> For this reason, multicenter studies using the same kit and reference ranges are needed.

In our study, 76.4% of female HCWs of childbearing age had anti-PT IgG levels below the protective maternal antibody level ( $\leq 30$  IU/ml). Similarly, in another study from Turkey, Esen et al.<sup>11</sup> reported that 51.7% of women of childbearing age had antibody levels of  $\leq 30$  IU/ml. The fact that most female HCWs of childbearing age do not have a protective maternal antibody level shows that they can be a source of infection not only for their patients but also for their own children.

We observed a significantly higher seropositivity rate among the HCWs in our study who worked 40–80 hours per week ( $p=0.03$ ). We believe

the low rate of seropositivity among HCWs working >80 hours per week can be explained by the fact that all of these HCWs were resident physicians who had worked at the children's hospital for one year or less. Similarly, Cunegundes et al.<sup>21</sup> reported that the risk of pertussis was highest among HCWs working 40 hours per week or more. In the present study, 21.3% of the HCWs had high-level anti-PT IgG positivity, suggestive of recent infection. This finding may be attributed to the increased risk of acquiring pertussis in HCW or the burden of disease in the community. Esen et al.<sup>11</sup> reported that 37.2% of their study group had antibody levels consistent with infection within the past few years. Ben Fraj et al.<sup>28</sup> reported high-level positivity in 11.4%, Urbiztondo et al.<sup>7</sup> in 7.8%, and Cunegundes et al.<sup>21</sup> in 6.4% of HCWs in their respective studies. Compared to studies in other countries, high-level positivity was more common in our study. Considering the cyclic pattern of pertussis, this may be related to the varying disease burden in different years and different countries. However, the WHO emphasized that this variability may result from different vaccination strategies utilized by countries in the past and present, and each country should consider local epidemiology while developing vaccination strategies.<sup>6</sup> The high-level positivity rates in our study, which indicate the persistence of circulation among HCWs, highlight the need for new vaccine strategies.

In our study, 63.6% of HCWs who used macrolide antibiotics due to chronic cough had serology suggestive of recent infection. In addition, high-level positivity was significantly more common in this group. It has been suggested that the use of empirical macrolides leads to misdiagnosis by masking clinical findings and decreasing the sensitivity of diagnostic methods in these HCWs. Therefore, to reduce the burden of pertussis and prevent transmission, pertussis should be suspected and serological methods used for diagnosis of adult patients with prolonged cough.

Rates of acute pertussis infection range from 1.3 to 4.5% in seroprevalence studies conducted among HCWs.<sup>7,17,27,28</sup> In our study, 1.8% had anti-PT IgG levels  $\geq 100$  IU/ml, indicative of active or very recent infection (within the last 12 months). One of these HCWs worked in the neonatal intensive care unit, and should have been isolated according to infection control guidelines. However, none of these three HCWs was suspected of a possible infection or isolated. Similarly, Koivisto et al.<sup>27</sup> reported that two nurses who had serological evidence of recent pertussis infection were not isolated. This finding is alarming, as asymptomatic transmission is known to be a risk factor for the spread of pertussis.

Vaccination coverage among HCWs varies from country to country according to vaccine strategies and awareness level. Some countries, such as the United States, Canada, Australia, the Netherlands, Germany, and the United Kingdom adopted booster dosing for all HCWs, while others, such as Austria, Finland, Norway, and Brazil, introduced Tdap only for those in contact with newborns and infants.<sup>30</sup> Nevertheless, it is also recognized that vaccine coverage among HCWs is still very low in all countries.<sup>31</sup> Although 74.0% of HCWs in our study stated that they considered a booster dose necessary and reliable, only 1.8% had gotten the booster dose. Similarly, Top et al.<sup>32</sup> reported that 76% of HCWs working in a children's hospital expressed an intention to get immunized, yet only 15% presented to a clinic where the pertussis booster vaccine was being provided free of charge. Urbiztondo et al.<sup>7</sup> determined that none of the HCWs in their study had received a booster dose, while Faruque et al.<sup>24</sup> reported that 23% had a booster dose.

The fact that 39.6% of HCWs in our study showed inadequate immunity highlights the need for the pertussis booster dose in HCWs. HCWs with acute infection act as infection sources for other workers and patients in the hospital. Most of the HCWs expressed a belief that the pertussis booster vaccine is necessary and safe;

however, the fact that hardly any of them had received the booster dose demonstrates that this awareness did not affect a change in behavior. All of these findings highlight that pertussis can occur in all age groups and that eradication cannot be achieved without effective adult immunization and surveillance.

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### Author contribution

The authors confirm contribution to the paper as follows: study conception and design: Selcen Özer and Vildan Avkan Oğuz; data collection: Selcen Özer; analysis and interpretation of results: Selcen Özer and Vildan Avkan Oğuz; draft manuscript preparation: Selcen Özer and Vildan Avkan Oğuz. All authors reviewed the results and approved the final version of the manuscript.

### Ethical approval

This cross-sectional study was approved by the Clinical Research Ethics Committee of Dokuz Eylül University hospital (decision number 13.07.2017, 2017 / 18-40).

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### Conflict of interest

None of the authors have a conflict of interest to declare.

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