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Original Article

Seroprevalence of IgG Antibodies against *Bordetella pertussis* in Different Age Groups in Tehran, Iran

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ABSTRACT

Background and Aims: **Pertussis is a highly contagious, vaccine-preventable disease. Determination of the seroepidemiology of pertussis makes possible the evaluation of pertussis immunity in a population. In this study, we determined the seroprevalence of *Bordetella pertussis* IgG antibodies in different age groups in Tehran, Iran.**

Materials and Methods: **Overall, 1101 subjects between ages of 8 months and 20 years were tested for the presence of pertussis toxin (PT), filamentous hemagglutinin (FHA) and different lipopolysaccharides (LPS) antibodies by ELISA.**

Results: **The overall prevalence of pertussis antibodies was 48% and the mean antibody level was 44± 47.7 U/ml. Over half (53.1%) of the children aged 8 months to 6 years were negative for pertussis antibodies. Pertussis antibodies rates and levels were significantly different between age groups ($P < 0.001$) and their significant elevations were observed with increasing age.**

Conclusion: **Up to half of the vaccinated children lacked an antibody response to vaccine, so using a more immunogenically effective vaccine to ensure sufficient immunity is essential. We showed that *B. pertussis* infection is on the rise in Iranian adolescents and young adults. Booster vaccination of this age group appears to be the most logical approach to disease prevention in adolescents and control the circulation of the organism.**

***Keywords: Bordetella pertussis*, Seroepidemiology, Iran**

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Introduction

Pertussis is a highly contagious respiratory disease, which is preventable with vaccine, and all age groups are susceptible to this infection (1). In children, pertussis is characterized by paroxysmal cough, whooping cough and post-tussive vomiting; but in adults the disease is often atypical and sometimes only manifested by a protracted cough (2).

In the pre-vaccination period, natural immunity was achieved early in the life and maintained through frequent contact with the organism, which acted as a natural booster. Routine mass vaccination of infants and children has been effective in decreasing the mortality and morbidity of the disease in children but has not eliminated the circulation of *Bordetella pertussis* (3, 4). Immunity following the vaccination or natural disease is not life-long and reinfection can occur, which causes increase of pertussis antibodies (5). Older children, adolescents, and adults are vulnerable to the infection due to waning of the vaccine-acquired immunity, and this causes the transmission of the disease to infants prior to the completion of their routine immunization, unless passively acquired antibodies are present in sufficient titers (6).

Vaccination by the triple diphtheria and tetanus toxoid and whole cell pertussis (DwPT) has been done in Iran for almost 50 years (7). The vaccination coverage in Iran was very close to 100% from 1997 based on Eastern Mediterranean Regional Office (EMRO) data (8). According to the current Iran National Immunization program, the pertussis vaccine is administered at the 2nd, 4th and 6th months of life, in combination with two booster doses, one administered in month 18 and the other between the years 4 to 6 as DwPT vaccine. The incidence of pertussis in Iran has decreased from 40% in 100,000 populations in 1978 to 0.5% in 100,000 populations in 2007 (9). Acellular pertussis (aP) vaccines have now been used in adolescents and adults and they are effective and safe for pertussis protection (10-12). The vaccine protection was estimated to be 92% (10). However, universal adult pertussis booster vaccination is controversial (13). In March 2006, the American Academy of Pediatrics published their recommendation regarding booster immunization of adolescents and recommended that adolescents between 11 to 18 years of age should receive a single dose of acellular pertussis vaccines combined with tetanus and diphtheria (DTaP) instead of tetanus and diphtheria toxoids vaccine for booster immunization (11). Vaccination of adolescents has been recommended in France, Germany, and Canada (14, 15).

Determination of the seroepidemiology of pertussis makes possible the evaluation of patterns of pertussis immunity in a population, and helps define the target population for pertussis booster vaccination.

Due to lack of information regarding the seroepidemiology of *B. pertussis* in Iran, in the current study, we aimed to determine the seroprevalence of IgG antibodies against *B. pertussis* in different age groups in Tehran, Iran.

Materials and Methods

In this cross-sectional study, 1101 subjects (606 males and 495 females) between ages of 8 months and 20 years residing in Tehran who visited in the pediatric and adolescent hospitals of Tehran were enrolled between January and September 2009. All study subjects had received whole-cell pertussis vaccine three times in the first year of life, followed by two boosters at the age of 18 months and 4-6 years. Subjects who either suffered from chronic diseases, immunodeficiency state or received intravenous immunoglobulin (IVIG) were excluded from the study. Informed consent was obtained from all cases or their parents. The study was approved by Pasteur Institute of Iran Ethics Committee.

Plasma samples were collected from cases and sent to the Clinical Research Department of Pasteur Institute of Iran. All samples were stored

at -80 °C prior to testing.

Plasma samples were tested for pertussis toxin (PT), filamentous hemagglutinin (FHA) and different lipopolysaccharides (LPS) IgG antibodies by ELISA. The commercial enzyme immunoassay kit was (IBL International, GmbH, Hamburg, Germany).

The procedure was followed as indicated by the manufacturer. According to the manufacturer's classification, values of <16 U⁄ml, 16–24 U⁄ml and >24 U⁄ml were considered as negative, equivocal and positive, respectively.

Statistical Analysis

The Chi-square, Mann Whitney and t^2-tests were used with the SPSS 13 Package program for statistical analysis (Chicago, IL, USA). Data are presented as mean ± SD or, when indicated, as an absolute number and percentage. Antibody values for the different age groups were analyzed by Kruskal–Wallis variance analysis. The 95% confidence interval (95 %CI) was calculated.

Results

A total of 1101 cases (606 males and 495 females) between ages of 8 months and 20 years were enrolled in the study. The cases were separated to four age groups: Group 1 (8 months-5.9 years; n =211), Group 2 (6.0-10.9 years; n = 361), Group 3 (11.0-15.9 years; n = 287) and Group 4 (16.0-20.9 years; n = 242).

The overall prevalence of pertussis antibodies was 48% (95% CI: 45%-51%). The mean antibody level was 44± 47.7 U/ml.

Pertussis antibodies prevalence rates according to age groups were as follows: Group 1; 46.9%, Group 2; 39.1%, Group 3; 46.3% and Group 4; 64.5%. Pertussis antibodies positivity in terms of age groups was significantly different from each other ($P < 0.001$). Except the 6-10 year age group, significant elevation in pertussis antibodies rates was observed with increasing age (Fig. 1). For all age groups, there was no statistically significant difference between genders regarding to pertussis antibodies positivity.

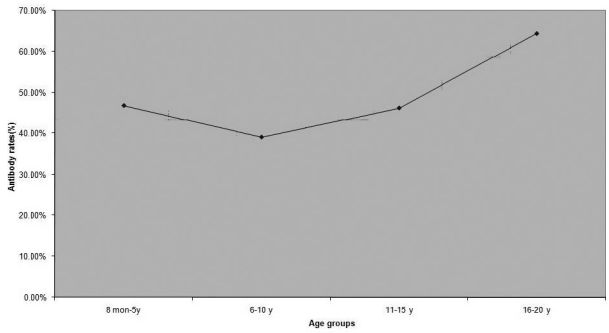

Fig. 1- Pertussis IgG antibodies rates in different age groups

The mean pertussis antibody levels according to age groups were as follows: Group 1; 30.5± 32 U/ml, Group 2; 36.5± 45.4 U/ml, Group 3; 43.4± 46.1 U/ml and Group 4; 67.8±55.6 U/ml. There was significant difference between age groups regarding mean antibody levels ($P < 0.001$) and significant elevation in pertussis antibody levels was observed with increasing age (Fig. 2). High-titer (≥150 U/ml) positivity was very low (3.3%) in the age group 8 months-6 years. With increasing age, high-titer positivity increased and reaching to its peak frequency (20.7%) in the group aged 16-20 years. Mean antibody levels in males and females were 45.2±48.4 U/ml and 42.6±47 U/ml respectively. There was not any significant difference between genders regarding to pertussis antibodies levels.

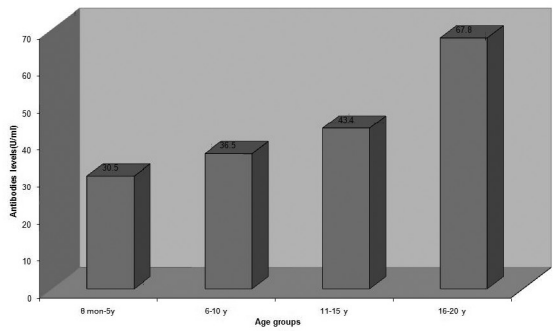

Fig. 2- Mean Pertussis IgG antibodies levels in different age groups

Discussion

In this study, the seroprevalence of IgG antibodies against *B. pertussis* in different age groups in Tehran, Iran was determined. The overall prevalence of pertussis IgG antibodies was 48% and the mean antibody level was 44± 47.7 U/ml. In our investigation, the significant elevations in pertussis antibody rates and levels were observed with increasing age and highest rates and levels were seen in cases aged between 16 and 20 years. In previous serological studies performed in different countries, pertussis protective antibodies were reported in a wide range of 30% to 97% (16-18). In other studies, it has also been shown that the pertussis seroprevalence increases with age (3, 4, 19, 20). As vaccine antibodies begin to wane 4 years after the last dose (21) and immunity to pertussis vaccine decreases to 0% to 20% over a 10-year interval (22); so the elevation of pertussis antibody rates and levels in our subjects reflects the acquisition of natural infection with *B. pertussis* following the joining cases to crowded community with a high probability of communicable disease. The older children and adolescences can then become a source of infection for neonates and young infants who have not yet completed their vaccination schedules.

In our survey, over half (53.1%) of the children aged 8 months to 6 years were negative for pertussis antibodies. It may be due to low immunogenicity of the licensed DTwP vaccines. A similar observation was also made in other studies in Italy and Greece, in which the efficacy and antibody responses of a whole-cell vaccine were unexpectedly low (23, 24). In the present study, 39.1% of children in the 6-10 year age group showed pertussis antibodies. This finding further supports that the whole-cell DTP vaccine that was usually administered to children 4-6 years old were not immunogenically effective. The lower immunogenicity of DTwP may be related to the bacterial strain used or the formulation protocol adopted for the vaccine preparation (25).

Few studies have been carried out about pertussis seroprevalence in Iran. A study in Isfahan reported 48% positive serology for IgG-PT in adolescents with prolonged cough (26). Hashemi *et al.* (27) reported 47.6% seropositivity of IgG-PT, with a mean level of 71.7 U/ml among the asymptomatic adolescent population in the west of Iran. In another study by Zarei *et al.* (25) in Iranian preschool children, the vaccine response and seroconversion for pertussis was achieved in 70.3% of the subjects. These conflicting data may be related to various factors such as the size and age of the study groups, and the demographic and epidemiologic factors.

In conclusion, our study showed that up to half of the vaccinated children lacked an antibody response to vaccine, so using a more immunogenically effective vaccine to ensure sufficient immunity is essential. In addition, we showed that *B. pertussis* infection is on the rise in Iranian adolescents and young adults. Booster vaccination of this age group with acellular pertussis vaccines appears to be the most logical approach to disease prevention in adolescents and control the circulation of the organism.

Conclusion

Before finalizing decisions concerning late childhood and adolescent immunization against pertussis, evaluation of the health benefits, risks, costs, and cost-effectiveness of pertussis vaccination in older children and adolescents in Iran is necessary.

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