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Seroepidemiology of Pertussis in a Set of Under One Year Old Iranian Children

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ABSTRACT

Introduction: Pertussis or whooping cough is one of the vaccine preventable diseases. The purpose of this study was to evaluate the seroepidemiology of pertussis in two groups of children (i.e. under 2 months and 2-12 months old) who had been admitted to Tehran Children Hospital. **Methods:** Sampling from the children was done along with completing a questionnaire including demographic information, clinical symptoms and the history of the parents coughing. The levels of IgG-Ptx antibody were then measured using the children's sera. **Results:** Overall, 10.8% of the children were not immune, 78.3% were immune, and 10.9% had recent pertussis infections. Moreover, 19.4% of the female and 13.1% of the male subjects had the infection. In the age group less than two months, 16.6% were infected. The likelihood of new infection among the children less than 2 months old was 1.2 times higher than the control group ($P < 0.004$). Fifty percent of the children who were diagnosed with cyanosis in their clinical examinations had a recent infection ($P < 0.001$). **Conclusion:** Pertussis appears to be endemic in Iran with children under one year old being at high risk of the infection. In this regard, maternal vaccination against pertussis for conferring passive immunity to the newborns could be considered as a protection measure.

INTRODUCTION

Pertussis or whooping cough is an acute infectious disease of the human respiratory tract, caused by a Gram-negative coccobacillus, named Bordetella pertussis. WHO estimations indicate that several million cases of B. pertussis infections occur annually, among which 300,000 deaths are caused by this pathogen [1]. Pertussis is mainly transmitted to other people through aerosols during coughing and sneezing in first 3 weeks of the illness [2]. In 72-83% of the children with pertussis, the source(s) of the infection are the child's parent(s) [3]. This disease is highly contagious and the rate of secondary infections among the family members is over 80% [4]. However, 46% of the secondary cases are asymptomatic [5]. Clinical symptoms are mainly due to pathogenic factors like secretion of B. pertussis toxins [6]. Acute illnesses with complications due to pertussis such as cyanosis and pneumonia are mainly observed in the unvaccinated children while more than 80% of the mortalities are reported for children under 4 months of age [7].
There are other pathogens such as Respiratory Syncytial virus, Adenovirus, Mycoplasma pneumonia, Chlamydia trachomatis, and Chlamydia pneumonia that can have respiratory symptoms similar to pertussis [8]. Moreover, long-term coughs due to asthma can sometimes be confused with pertussis [9]. Pertussis can be distinguished from similar diseases by presence of pertussis toxin (PT) which is a unique component of B. pertussis. In all acellular and whole cell vaccines against pertussis, antibody against PT is induced in the infected people and also in individuals vaccinated against the disease. In Iran, whole cell pertussis vaccine is administered after 2 months of age, followed by boosters at 4 and 6 months and also at ages of 4 and 6. The levels of anti-PT antibodies are measured and used for serological diagnosis of pertussis [10]. Measuring IgG-PT, IgM-PT and IgA-PT immunoglobulins in sera of pertussis patients of various age groups and the sera of patients with a history of pertussis vaccination shows that IgG-PT is more sensitive than the other two anti-PT immunoglobulins [11, 12].
Moreover, it has been reported that combining IgA-PT and IgG-PT results does not lead to increased test sensitivity [13, 14]. Considering the high mortality of pertussis reported by The Iranian Ministry of Health and Communicable Diseases Management Center, we evaluated pertussis seroepidemiology in two groups of under one-year-old children (i.e. under 2-months and aged 2-12 months), admitted to Tehran Children Hospital, using IgG-Ptx antibody.

MATERIALS AND METHODS

Sampling: Based on estimated high prevalence of pertussis in young children and similar study situations [15], a sample size of 120 was chosen for this study. The inclusion criteria were being under one year old, coughing for more than 3 weeks, not being received any acellular pertussis vaccine by the mothers during their pregnancy and delivery and lack of immunodeficiency diseases in the children. Samplings were

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done at Tehran Children Hospital which is a referral center for children from all medical centers in Tehran and Iran. Consent forms were completed and obtained from the parents of the children. Ethical approval of the study was obtained from Institute Pasteur of Iran's Ethics Committee (approval #: 96.0201.20877). The samplings were done during 1 year. Two age groups, namely Group 1 with babies less than 2 months and Group 2 with babies aged 2-12 months, were examined in this study. Blood samplings were accompanied by completing a questionnaire with demographic information including date of birth, date of diphtheria, pertussis, and tetanus (DTP) vaccination, and the number of vaccine doses received, history of the parent's coughing for more than 3 weeks and the clinical symptoms of the disease, namely cyanosis and post-tussive vomiting. After collecting the sera, they were kept at -80°C until ELISA was performed.

Measuring IgG-Ptx by ELISA: The vesicles were extracted as described previously [9, 10]. The serologic pertussis test was done for all subjects. Measuring IgG-Ptx antibody was done by ELISA on the sera taken from each subject. The ELISA kit was from IBL Co., (Germany). According to the manufacturer and WHO recommendations [12], anti-PT IgG values under 10 IU/ml were interpreted as non-immune, 10–100 IU/ml were considered as immune, and above100 IU/ml were regarded as acute pertussis infection or recently vaccinated.

Statistical Analysis

The data was analyzed by SPSS ver. 24 (USA). Chi-square test or Fisher's exact test were used for univariate analysis and multivariate logistic regression for adjusting the effect of dummy variables on the incidence of pertussis. The significance level used was $P < 0.05$.

RESULTS

Among 120 subjects participated in this study who were divided into group 1 and group 2, 36 (30%) were female babies and 84 (70%) were male babies. Our obtained results indicated that19.4% of the females and 13.1% of the males had recent pertussis infection (Table 1). The age of the participants had a high correlation with the epidemiology of the disease, immunization and vaccination, as follows. In Group 1, 16.6% and in Group 2, 14.1% were infected. Among the age groups, 66.7% of the children in Group 1 and 84.6% of children in Group 2 were immune to pertussis. The likelihood of new infection among the children in Group 1 was 1.2 times higher than Group 2. This difference was statistically significant ($P <0.004$; Table 1).The participants were also analyzed based on their residence location. Our data indicated that among 120 participants, 82 (68%) were living in Tehran and the rest (32%) were from the other provinces. Moreover, 12.2% of Tehran residents had a recent pertussis infection, whereas 5.3% of children in other provinces had a recent infection. The differences observed between the residents of Tehran and the other provinces were not statistically significant (Table 1).

Comparing the results of those who had received pertussis vaccine against those who had not, we observed that 16.6% of children who had not received the vaccine at all had a recent infection, whereas children who had received 3 doses of the pertussis vaccine (i.e. Group 2, in months 2, 4 and 6) showed 14.1% recent infections which was statistically significant ($P < 0.004$; Table 1). The odds of a recent infection were 1.2 times higher in those who had not received the vaccine compared to the ones who had received it.

Previous studies indicate that parents and other family members of the pertussis patients have a significant role as a source of infection for children under one year of age[16]. Thus, in our study, this variable was examined in the two study groups. Our results indicated that 41.6% of the children in this study with parents coughing more than 3 weeks had recent infections, whereas 1.3% of children whose parents had no more than 3 weeks of coughing had a recent infection which was statistically significant ($P < 0.00001$;Table 1). The likelihood of developing pertussis in the children whose mothers had suspicious clinical symptoms of pertussis was 55 times higher, compared to the parents of children whose parents did not cough. Hence, the incidents of children in Group 1 having recent pertussis infections were highly correlated with their parents' illness.

Cyanosis is one of the main symptoms of pertussis in children. This variable was examined and it was observed that 50% percent of the children with cyanosis had recent pertussis infection while the recent infection in the children with no cyanosis was significantly lower (only 4.4%; $P < 0.001$; Table 1). Our results indicated that the possibility of developing acute pertussis in a child with cyanosis was 22 times more than those without cyanosis in their clinical examinations. Thus, cyanosis can be considered as a good marker for the suspicious pertussis cases. Another major symptom of pertussis in children under 1 year of age is post-tussive vomiting[17]. In this study, 46.8% of the children with this symptom had a recent infection; whereas, those without post-tussive symptom had a significantly lower incidences of a recent infection (10.5%; $P <0.001$; Table 1). Altogether, the likelihood of pertussis infection with post-tussive vomiting symptom was estimated to be 7 times more than the asymptomatic children.

DISCUSSION

In this study which investigated the seroepidemiological characteristics of pertussis cases and its accompanied clinical symptoms in young children in a Tehran hospital over a year, it was observed that pertussis was more prevalent in male babies than the female ones. Moreover, the cases of the disease were more in Group 1 (i.e. less than 2 months) than in Group 2 (i.e.2-12-month-old) babies. In terms of location of residence, more cases were residents of Tehran. The children without a history of vaccination were more likely to have pertussis than the vaccinated ones. In terms of the parents symptoms, coughing for more than 3 weeks of a parent of a child with less than two months of age, could be considered as an indicator of the child having pertussis. The age pattern of pertussis in children was in line with previous studies by Shahcheraghi et al. across Iran [18], Mousazadeh et.al. in city of Sari[19] in Mazandaran province of Iran, and Alessandro et al. in Brazil [15].

In a study by Bellettini et al. [20] in Brazil in which the researchers examined 222 of suspected pertussis-related individuals from September 2011 to January 2013, 72.5% of the subjects were reported to have pertussis which 60.9% of them were under one year of age. The researchers then have proposed that cyanosis among children younger than 6 months could be considered as an independent predictor of pertussis.

In our study, cyanosis along with high IgG-ptx antibody titers in children under 2 months was an independent predictor of pertussis. Therefore, it would be suggested that in laboratories with no culture and PCR facilities, IgG-Ptx titers along with clinical symptoms could be considered for diagnosis of pertussis, especially for coughing children under two-months old. PT antigen is expressed only in B. pertussis[10] . Previous

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pertussis studies have reported that 92.2% anti-Ptx IgG sensitivity by ELISA for serologic diagnosis of pertussis [21, 20]. Comparison of anti-Ptx IgG with antibodies against other pertussis vaccine antigens have indicated that antigens other than PT have low sensitivity[12]. Thus, IgG-ptx was used for evaluation of seroepidemiology in this study.

Similar infection statistics in recent years have also been reported in Turkey. For instance, in a serological study in Izmir, Turkey, the antibody levels of 399 healthy individuals aged 6 months to 60 years have been analyzed [22]. The results of this research have revealed that IgG antibody levels in 8.5% were less than 10 EU/ml (i.e. non-immune), in 68.2% from 10 EU/ml to 100 EU/ml (i.e. immune), and in 23.3% were more than 100 EU/ml (i.e. acute infection). Moreover, another serological study in Ankara, Turkey, has shown that 9.7% of the studied population had more than 100 EU/ml IgG-ptx, indicating acute infections [23]. Meanwhile, in our study, among 120 subjects, 13 (10.8%) were not immune, 94 (78.3%) were immune, and 18 (10.9%) had recent infections. Therefore, the prevalence of pertussis in Turkey seems to be similar to that of Iran, and antibody levels above 100 EU/ml suggest that B. pertussis strains are circulating among the population of the two neighboring countries.

Based on a recent study, parents and other family members of the pertussis patients have a significant role as a source of infection for children under one year of age as follows. Examination of infants' home contact with laboratory-confirmed outpatient infections during pertussis outbreaks in England and Wales [16] has shown 220 contacts among 63 families. Mothers in 38% of the cases and then siblings (31%) and fathers (10%), were the probable sources. Likewise, 41.6% of the children in our study whose parents had coughing symptoms for more than 3 weeks had a recent infection (Table 1). The likelihood of pertussis infection in children whose mothers were suspected to have pertussis was 55 times higher than those of children whose parents had no suspected pertussis coughing. Therefore, the involvement of children less than two months of age with recent infection was significantly related to their parents' state of health.

It has been suggested that immunization during pregnancy has a key role in preventing the infant's disease through passive immunization at birth and reducing maternal exposure to the infant [16]. Nowadays, vaccination coverage in Iran is 99% according to the statistics of the Ministry of Health and Communicable Diseases Management Center [24]. However, the results of this study show that 11 cases (14.1%) were the vaccinated children who were infected with pertussis infection. The possible reason to explain this could be that antigens in the vaccine strain used in Iran are different from the circulating pertussis strains in the community. Interestingly, studies by Shahcheraghi et al. show that 48% of B. pertussis strains isolated from Iranian patients had allelic differences in ptxP3, ptxA1, prn2, fim 2-1, fim3-2, and cya2 antigens [25, 26]. In conclusion, we believe that the prevalence of the disease in children under one year of age can be due to inadequate or incomplete vaccination in this age group. Children under 2 months are closely in contact with adults whom can be considered as a source of the infection. Thus, screening the parents of children younger than two months for pertussis could have a significant role in reducing the incidence of the disease at this age. According to the results of this study and the previous ones conducted in Iran, one can state that pertussis is probably endemic in Iran; thus, there is a potential risk of transmission of the infection to susceptible individuals, especially the infants. Therefore, it appears that maternal vaccination to confer passive immunity to the newborn babies may be helpful in resolving this problem.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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