

The Incidence of *Bordetella Pertussis* Infections in Jahrom City, Southern Iran

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Abstract

Background: *Bordetella Pertussis*, known as the causative agent of whooping cough, is one of the leading causes of recurrent persistent cough at all ages, even in vaccinated individuals.

Methods: A total number of 110 patients coughing for at least two weeks who were admitted to clinical centers in Jahrom, Iran, were included in this cross-sectional study. For this purpose, blood samples were collected from these individuals at two stages, i.e., at the beginning of the study and on the 21st day. Afterward, anti-pertussis toxin (PT) immunoglobulin G (IgG) was measured in serum samples via the enzyme-linked immunosorbent assay (ELISA). The given cases were further evaluated in terms of age, gender, occupation, place of living, and family size.

Results: Out of 110 patients recruited in this study, 77 cases were female (70%). Also, only seven patients were shown to be serologically positive (6.4%). Moreover, no significant association was observed between pertussis incidence rate and the study variables, namely, age, gender, occupation, residency area (urban or rural), and family size ($p>0.05$).

Conclusions: This study aimed to emphasize pertussis occurrence in individuals who merely present persistent cough without typical symptoms. This requires the physicians to conduct more precise assessments along with more rapid diagnostic methods.

Background

Pertussis or whooping cough is considered to be a highly contagious respiratory disease caused by the gram-negative bacterium *Bordetella*, and is one of the major causes of recurrent lingering cough at all ages, even in vaccinated individuals. The risk of developing the disease increases as a longer time elapses since vaccination [1, 2]. The underlying cause lies behind the fact that vaccine-induced immunity is limited (last maximumly for 12 years); hence, vaccinated children are immune to the disease but adults are either deprived of such immunity or possess a weaker immunity [3]. Outbreaks of this epidemic generally occur every other 3-5 years [4, 5]. Over the past few years, pertussis incidence rate followed an ascending trend in many countries including those with a high level of immunization coverage [6]. Similarly, it is estimated that there are about 16 million cases of the disease worldwide annually from which 95% of them reported from developing countries, and it leads to a mortality rate of 400,000 individuals [7-9]. The serologic test of anti-pertussis toxin (PT) immunoglobulin G (IgG) (PT-IgG) has been introduced as a gold-standard test for definitive diagnosis of pertussis by the Council of State and Territorial Epidemiologist (CSTE) [10].

Besides, numerous studies have reported a rising trend in pertussis incidence rate in youth and adults [11-13]. Accordingly, the results of serological tests have further established that more than 10-20% of adults suffering from chronic cough, lasting two or three weeks or so, are more likely to be infected with pertussis [14,15].

For example, in the study by Teepe et al. (2015), out of 3074 babies below one year of age with a cough lasting for more than two weeks and at least one clinical symptom such as paroxysms, inspiratory whoop, or post-tussive emesis, 3% of the cases were reported to be infected with pertussis in 12 European countries [16]. They had finally concluded that adults could be the main sources of transmission of the disease, while they are mostly ignored in early diagnosis by physicians [17]. In another study conducted by Karagul et al. (2015) had revealed that 3 (1.4%) and 15 (7%) cases had been positive, based on culture method and polymerase chain reaction (PCR), respectively; as they investigate a total number of 240 patients with cough symptoms for at least two weeks in Turkey. They correspondingly emphasized that *Bordetella pertussis* needs careful investigations in the differential diagnosis of recurrent lingering cough among adults, and thus diagnosis and treatment of this infection could prevent its transmission [18].

This subject is limitedly addressed in the literature worldwide as well as in Iran, hence the present study aimed to investigate the pertussis incidence rate in patients who were admitted to clinical centers of Jahrom, Iran.

Methods

Study Design and Statistical Population

This descriptive cross-sectional study was conducted on a total number of 110 patients who referred to clinical centers of infectious diseases affiliated to the hospitals of Jahrom University of Medical Sciences in Iran from January to March 2012.

The eligibility criteria required for the participants to enter the study were as follow: cases should manifest persistent cough for more than two weeks, should have not received vaccinations since the last five years, and should be in the age range of 12-72 years. Moreover, patients who were affected by allergy, sinusitis, gastroesophageal reflux disease (GERD), chronic obstructive pulmonary disease (COPD), and asthma as well as those who were taking medications particularly antibiotics were excluded from the study.

Data Collection and Measurements

All the patients meeting the eligibility criteria at the time of the study were recruited upon obtaining written consent and research conditions were further explained. First, patient demographic data (i.e., gender, age, occupation, place of living, and family size) were recorded and entered into specific forms for collecting the mentioned data. Then, venous blood (2 cc) was collected from each patient (twice; once at the beginning of the study and then at the 21st day of follow-up). The samples of patients' serum were also kept at -20°C for serological tests. Corresponding to the manufacturer's protocol, Anti-PT IgG concentrations were assessed employing a commercial ELISA kit (Euroimmun, Lübeck, Germany). While possessing a specificity of 90% and a 91% sensitivity, this kit is believed to be the uppermost among eleven PT antibody kits that are available in the market [19]. Anti-PT IgG level of ≥ 62.5 IU/mL was adjusted to establish seropositivity[20].

Statistical Analysis

The data obtained were analyzed in IBM SPSS Statistics software (version 21) through descriptive and analytic tests (namely, Chi-square test and Fisher's exact test). The significance levels in all tests were considered to be $p<0.05$.

Results

Totally, 110 patients were qualified to participate in the study who were admitted to Honari Clinical Center Paymaiye Clinical Center located in Jahrom. Regarding gender distribution, 33 cases were male (30%) and 77 patients were female (70%). Our quantitative analyses revealed that 7 patients (6.4%) among them had elevated titers of anti-PT-IgG at days 0 and 21, including three men (9.1%) and four women (5.2%) who were infected with pertussis. Even though the percentage of the infected men was higher than that of women, this difference proved no statistical significance ($p=0.672$) (Table 1).

The subjects were also divided into six age groups (Table 1). Accordingly, no cases with pertussis were detected in age groups 1 and 6 (0%), whereas the most frequent affected individuals reported from age group 2 (15.8%). There was also no significant relationship between the incidence rate of pertussis and the variable of age ($p=0.565$). Regarding the occupation of the participants, the percentage of positive cases (57.14%) was evidently higher among housewives (4 housewives out of 7 positive cases), however, this difference was not significant ($p=0.07$). With regard to the residency area (urban or rural areas), individuals living in urban areas accounted for the highest percentage of pertussis (8.2%), however, this difference was not significant again similar to the previous variable ($p=0.420$). For a more comprehensive analysis, the patients were further allocated into three groups based on the size of their family (Table 1). Although most of the positive cases were found in group 2 (57.14%), no significant difference was observed between the incidence rate of pertussis and family size ($p=0.409$).

Table 1 Trends of pertussis incidence rate in patients admitted to clinical centers in the city of Jahrom based on demographic data

| Variable | Incidence rate (Frequency) | Positive | Negative |
|------------------------|----------------------------|-----------|------------|
| Gender | | | |
| <i>Female</i> | 77 (70%) | 4 (5.2%) | 73 (94.8%) |
| <i>Male</i> | 33 (30%) | 3 (9.1%) | 30 (90.9%) |
| Age group | | | |
| <i>Group 1 (10-20)</i> | 7 (6.4%) | 0 (0.0%) | 7 (6.4%) |
| <i>Group 2 (21-30)</i> | 19 (17.3%) | 3 (15.8%) | 16 (84.2%) |
| <i>Group 3 (31-40)</i> | 33 (30%) | 2 (6.1%) | 31 (93.9%) |
| <i>Group 4 (41-50)</i> | 28 (25.5%) | 1 (3.6%) | 27 (96.4%) |
| <i>Group 5 (51-60)</i> | 19 (17.3%) | 1 (5.3%) | 18 (94.7%) |
| <i>Group 6 (61-72)</i> | 4 (3.6%) | 0 (0.0%) | 4 (100%) |
| Occupation | | | |
| <i>Student</i> | 6 (5.5%) | 0 (0.0%) | 6 (100%) |
| <i>Military man</i> | 1 (9%) | 1 (100%) | 0 (0.0%) |
| <i>Employee</i> | 13 (11.8%) | 1 (7.7%) | 12 (92.3%) |
| <i>Self-employed</i> | 23 (20.9%) | 1 (4.3%) | 22 (95.7%) |
| <i>Housewife</i> | 67 (60.9%) | 4 (6%) | 63 (94%) |
| Residency area | | | |
| <i>Urban area</i> | 73 (66.4%) | 6 (8.2%) | 67 (91.8%) |
| <i>Rural area</i> | 37 (33.6%) | 1 (2.7%) | 36 (97.3%) |
| Family size | | | |
| <i>Group 1 (1-3)</i> | 36 (32.7%) | 3 (8.3%) | 33 (91.7%) |
| <i>Group 2 (4-6)</i> | 53 (48.2%) | 4 (7.5%) | 49 (92.5%) |
| <i>Group 3 (7-13)</i> | 21 (19.1%) | 0 (0.0%) | 21 (100%) |

Discussion

In the present study, elevated serum IgG titers were observed in 4.6% of the patients with coughing for more than two weeks. However, several studies carried out in developed countries have so far indicated that pertussis is among one of the common most causes of frequent and violent cough (with an

incidence rate of 2.9-32% in adults), but physicians are unfortunately often unaware of this disease [18,21,22].

In this respect, Ghorbani et al. (2016) investigated the epidemiological characteristics of pertussis among Iranian suspected patients and further reported that 6.6% of the cases had shown positive test results similar to results obtained in the present study [23].

The results of another research by Ghatasloo and Mohammadzadeh-Asl (2017) had further demonstrated that the overall positivity of *Bordetella pertussis* in serum samples from Asians, from 2000 to 2015, was by 36%, but the given value in Iran was 38.4%. This incidence percentage was higher than that reported in the present study [24]. Similarly, in another study by Rabiee et al. (2015), pertussis occurrence had been reported to be 20.44% among patients who referred to Tehran Diagnostic Medical Transplant Laboratory [1].

Similar studies had been correspondingly conducted in other countries on a global scale, including that by Pimentel et al. (2015). Consistent with our study, they investigated 192 patients suspected of pertussis using the culture method and PCR in Brazil and estimated the incidence rate of 21%. In contrast to our findings, the investigation of Lee et al. (2018), examining clinical nasopharyngeal and blood samples of 686 patients with cough, had further shown that the incidence of *Bordetella pertussis* attained 13.6% in seven distinct places in the United States between 2007 and 2011 [10], which was higher than that of the present study. However, these results had been in agreement with the findings of the studies by Nirada Siriyakorn et al. (2016) in Thailand (18.4%) [15], Sonmez et al. (2016) in Turkey (9.7%) [14], as well as Kayina et al. (2015) in Uganda (20%) [25].

Additionally, in the study by Yeng et al. (2017), it had been estimated that 3.5% of children under 5 years of age residing in Southeast Asia in 2014 had been totally affected with pertussis, which led to mortality in approximately 0.67% of the cases [26]. This finding was lower than that reported in the present study. Also, in another 5-year investigation by Masseria et al. (2017) in the United States, the pertussis incidence rate in children under 12 months of age attained 117.7 per 100,000 people/years wherein the highest incidence rate had been observed in 3-month-old infants (247.7 per 100,000 people/years) [27]. It seems that the discrepancy in incidence rates reported in different studies might be associated with epidemiology of the disease in each region, variety of samples, time of the study (different seasons), and age groups.

Another analysis performed in this study was the relationship between age and pertussis incidence rate, but it did not show any statistical significance. Regarding the prevalence of different age groups, most of the cases were observed in the second age group (21-30 years old, 15.8%) followed by age group 3 (31-40 years old, 6.1%). Studies conducted in different countries had further reported different incidence rates according to age groups. With reference to a study in Turkey, the pertussis incidence rate in individuals aged 13-19 years was the highest [28], however in the survey by Skoff et al. (2018), the highest incidence rate was reported among infants (75.3 cases per 100,000 people) [29]. On the other hand, some studies had addressed the peak incidence rates in the age group over 60 years [30,31].

It is of note that adolescents and young adults with lower levels of protective antibodies against PT may experience pertussis recurrence. There are several reasons for coughing in a vaccinated population including inadequate vaccination, changes in vaccine quality, types of vaccines, immunosuppression following initial vaccination, demographic changes, and adaptation of bacteria and their acquired vaccine-driven resistance, misdiagnosis, as well as lack of reports due to absence of specific symptoms of pertussis and subsequently its transmission to vulnerable individuals. Despite milder manifestations of the disease in older children and adults, some scientists argue that pertussis can be multifaceted in adults [30-32]. Thus, the possible reasons for the difference in the peak incidence rate of pertussis in various age groups can be attributed to variations in sample size, immune response dynamics, and community transmission.

The gender difference was also among other factors investigated in this study. In this regard, the pertussis incidence rate was higher in males than that in females, although this difference was not noticeable. Consistent with our results, a cross-sectional investigation conducted at Shahid Beheshti Hospital in the city of Zanjan, Iran, had also found that the number of patients with a positive culture for pertussis was higher in men compared to women (26.3% vs. 12.1%) [33]. South Korean scientists also conducted a study to assess epidemiological characteristics of pertussis in adults and reported that test results (viz. culture method and PCR) in 6.9% of the patients were positive and the ratio of women to men obtained 356 to 134 [34]. However, these findings were in conflict with those in the present study, but they supported the results reported by Ghorbani et al. (2016) [23]. One possible reason for such a discrepancy was the recruitment of different age groups of populations in these studies.

Although pertussis incidence rate in individuals living in urban areas was higher than that of subjects residing in rural districts, no significant difference was noticed. These slight variations might be attributed to patients' access to health care centers, earlier diagnosis, level of vaccination coverage, population density, and more transmission routes of the disease. The study by Ghorbani et al. (2016), determining the epidemiological pattern of pertussis in Iran between 2011 and 2013, similarly reported that there is no significant difference between rural and urban populations [23], which was in accordance with our findings.

In total, no emphasis had been laid on gender and residency area in the literature. It seems that most differences associated with these two variables might be related to extent of immunization.

Occupation and family size were another two variables in this study. Pertussis occurrence was higher among employees and military men compared with other occupations in the present study, and it was demonstrated to be more common in families of 1 to 3; however, no statistically significant difference was found between these variables and prevalence of the disease. This finding was also reproduced in the studies of Tarlo et al. (2016) and Lytras et al. (2015). The given studies had suggested that factors such as excessive exposure to dust, gases, or smokes, and cigarette smoke could be accompanied by an increased occurrence of cough or sputum secretion, although chronic cough could be often based on non-occupational types [35, 36]. While many surveys addressed no association between family size and

pertussis incidence rate, exposure to family members suffering from a cough or sharing beds with them play a remarkable role in the development of pertussis manifestations [25].

Among the most noticeable limitations in the current study was the fact that no PCR was performed on the patients suspected with pertussis, and thus could lead to false-positive in serologically confirmed cases in laboratories. The second limitation of the study was the difficult recruitment of the patients for sample collection at day 21 (day 0 and day 21), which was resolved through frequent follow-up and exclusion of the reluctant patients for 2nd sampling.

Conclusions

In conclusion, pertussis is an acute respiratory infection and considered to be highly contagious. Less known differential symptoms such as lingering cough in adults have caused physicians to neglect this disease during diagnosis at an early stage. The present study aimed to highlight the presence of this disease in individuals merely with a prolonged cough but without typical symptoms. It can be also concluded that pertussis still requires more rapid diagnostic methods.

Abbreviations

COPD: Chronic obstructive pulmonary disease; CSTE: Council of State and Territorial Epidemiologist; ELISA: enzyme-linked immunosorbent assay; GERD: gastroesophageal reflux disease; IgG: immunoglobulin G; PCR: polymerase chain reaction; pertussis toxin

Declarations

Ethical approval of the study

Written informed consent was obtained from the patient in our study. The purpose of this research was completely explained to the patients and was assured that their information will be kept confidential by the researcher. The present study was approved by the Medical Ethics Committee of the academy.

Consent for publication

Consent was obtained from the patients regarding the publication of this report.

Availability of data and materials

SPSS data of the participant can be requested from the authors. Please write to the corresponding author if you are interested in such data.

Competing interests

The authors declare that they have no competing interests.

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Authors' contribution

RR designed the study while NT collected the data and drafted the manuscript. RS proofread and edited the manuscript. All authors proofread and approved the final version of the manuscript.

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Ethical Considerations

Before recruiting the patients in this study, the research process was explained and informed consent was obtained. The current study was conducted in accordance with the principles of the Helsinki Declaration to maintain the patients' privacy in all stages of the study. This project was funded by the researchers and the patients were incurred for no additional costs. This study was granted permission by the Vice Chancellor's Office for Research and Technology at Jahrom University of Medical Sciences and further approved by the Ethics Committee of this university under the code of ethics no IR.JUMS.REC.1390.020.

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