

Pertussis Prevalence in Korean Adolescents and Adults with Persistent Cough

Soo Young Lee,^{1,2} Seung Beom Han,^{1,2}
Jin Han Kang,^{1,2} and Ju Sang Kim³

¹Departments of Pediatrics, and ²Vaccine Bio Research Institute, College of Medicine, The Catholic University of Korea, Seoul; ³Department of Pulmonology, The Catholic University of Korea, Incheon St. Mary's Hospital, Incheon, Korea

Received: 23 November 2014

Accepted: 17 February 2015

Address for Correspondence:

Jin Han Kang, MD

Department of Pediatrics, Seoul St. Mary's Hospital, The Catholic University of Korea, 222 Banpo-daero, Seocho-gu,

Seoul 137-701, Korea

Tel: +82.2-2258-2828, Fax: +82.2-537-4544

E-mail: kjhan@catholic.ac.kr

Funding: This study received funding support from

GlaxoSmithKline Biologicals (Grant No. 5-2010-D0341-00002).

We investigated the prevalence of pertussis in Korean adolescents and adults with persistent cough. Study population was adolescents (aged 11–20 yr) and adults (≥ 21 yr old) who showed persistent cough of 1–8 weeks' duration. Pertussis was diagnosed by culture, polymerase chain reaction (PCR), and serology. A total of 310 subjects participated in this study, and 76 cases (24.5%) met the criteria for laboratory-confirmed pertussis. The majority of the pertussis cases (66/76) were confirmed by serology, while 3 cases (1.0%) were diagnosed with culture, and 10 cases (3.2%) were detected with PCR. Of the 76 subjects diagnosed with pertussis, 20/86 cases were adolescents and 56/224 cases were adults. Neither adolescents nor adults received adolescent-adult booster against pertussis within the previous 5 yr. Pertussis can be a primary cause of persistent cough in Korean adolescents and adults.

Keywords: Pertussis; Adolescent; Adult; Cough; Korea

In Korea, maintaining a high vaccination rate with diphtheria-tetanus-acellular pertussis (DTaP) in infants and children has successfully led to a decreased prevalence of the relevant diseases (1, 2). No cases of diphtheria have been reported since 1987 and a low incidence rate of tetanus with around 10 cases per year has been maintained since the 1990s (3). On the other hand, the number of reported cases of pertussis has been recently on the rise (4).

Immunity to pertussis acquired from either natural infection or vaccination does not last throughout the lifetime. Therefore, as with diphtheria and tetanus, pertussis requires additional vaccinations (5). Even if an individual was properly vaccinated with DTaP during childhood, the acquired immunity would not last without additional vaccinations for pertussis during adolescence and adulthood, which makes the individual susceptible to pertussis infection (6). These adolescents and adults act as a significant infectious source of pertussis in infants (5, 6). To prevent this phenomenon, a tetanus toxoid, reduced diphtheria and acellular pertussis (Tdap) vaccine has been included in the National Immunization Program of Korea since 2012. Currently, Tdap vaccine is recommended as the first booster immunization for individuals aged 11–12 yr, instead of the previous diphtheria and tetanus toxoids (Td) vaccine (7).

This study was conducted prospectively to investigate the prevalence of pertussis in adolescents and adults with persistent

cough in Korea. The subjects in this study were adolescent and adult patients with persistent cough, who visited the departments of pediatrics or pulmonology of two university hospitals in Korea, Seoul St. Mary's hospital and Incheon St. Mary's hospital, between December 2009 and December 2011. Included subjects were adolescent (aged 11–20 yr) and adult (≥ 21 yr old) patients who showed persistent cough of 1–8 weeks' duration. Patients were excluded if they had an underlying disease associated with persistent cough, such as asthma, tuberculosis, lung cancer, chronic obstructive lung disease, or sinusitis (8, 9). The study was approved by the Institutional Review Board of the Catholic University of Korea (XC09EIMI00990). Informed consent was exempted by the board.

We obtained demographic and clinical manifestations, and information on immunization status of the subjects. Also, nasopharyngeal aspirates (NPA) and blood samples for each subject were collected. It was determined as the same criteria for laboratory-confirmed pertussis case as previously reported (10). In brief, the subjects were applicable to one of the following laboratory tests: 1) culture positive for *Bordetella pertussis* of NPA; 2) PCR positive for *B. pertussis* of NPA; or 3) seropositive results which defined as anti-pertussis toxin (PT) titer > 24 EU/mL of ELISA kit (IBL International GmbH, Hamburg, Germany) according to the manufacturer's recommendation. Laboratory tests were performed at the Vaccine Bio Research Institute of

Table 1. Laboratory-confirmed pertussis cases among patients with persistent cough

	Culture positive (%)	PCR positive (%)	Seropositive (%)	Any positive (%)
Adolescent (n = 86)	0 (0.0)	6 (7.0)	20 (23.3)	20 (23.3)
Adult (n = 224)	3 (1.3)	4 (1.8)	56 (25.0)	56 (25.0)
Total (n = 310)	3 (1.0)	10 (3.2)	76 (24.5)	76 (24.5)

the Catholic University of Korea. Statistical analyses were performed using the SPSS statistical analysis package (version 17.0 for Windows). Comparisons of proportions were tested using chi-square test and Fisher's exact test, as appropriate, and the criterion for statistical significance was P value < 0.05 .

A total of 310 subjects participated in the study; 86 adolescents (aged 11-20 yr) and 224 adults (≥ 21 yr old). Among the 310 cases, 76 cases (24.5%) met the criteria for laboratory-confirmed pertussis case. The majority of the pertussis cases (66/76) were confirmed by serology, while 3 cases (1.0%) were diagnosed with positive culture, and 10 cases (3.2%) were detected with PCR. All culture positive cases showed the PCR positive and the seropositive as well. All PCR positive cases also showed seropositive. In the adolescent group, higher PCR positive rate was observed than in the adult group. However, none in the adolescent group was proved to be pertussis case on the culture (Table 1).

Of the 76 cases diagnosed with pertussis, 20/86 cases were adolescents and 56/224 cases were adults. When subjects were divided into seven age groups; 11-20 yr, 21-30 yr, 31-40 yr, 41-50 yr, 51-60 yr, 61-70 yr, and ≥ 71 yr, the group aged 11-20 yr (26.3%) showed the highest proportion of pertussis cases than other six age groups; 6.6%, 15.8%, 13.2%, 15.8%, 17.1%, and 5.3%, respectively.

The difference of clinical and laboratory data was compared between 20 adolescents and 56 adults diagnosed with pertussis. All adolescents were confirmed by medical records to have received pertussis vaccine 4 or 5 times by the age of 6 yr. There were no available medical records of the majority of the enrolled adults, to prove their immunization status. Within the previous 5 yr, neither adolescents nor adults with pertussis received adolescent-adult boosters against pertussis (Tdap vaccine). The adolescent group showed shorter duration of cough ($P < 0.001$), and higher mean antibody titer ($P = 0.004$) than the adult group (Table 2).

One thing that should not be overlooked in pertussis epidemiology studies is the investigated prevalence of pertussis was highly dependent on the serologic definition (11). In clinical practice, an individual is considered to have protective immunity against pertussis if ELISA antibody titer against pertussis toxin (PT) or filamentous hemagglutinin (FHA) is ≥ 20 -30 EU/mL (12, 13). However, due to lack of standardized method to measure pertussis antibodies, test values may vary between laboratories (6, 8). To help resolve this limitation, guidelines have been published as criteria for the assessment of protective immunity

Table 2. Characteristics of persistent cough patients diagnosed with pertussis

	Adolescent (n = 20)	Adult (n = 56)
Age, mean \pm SD (yr)	12.20 \pm 2.89	48.89 \pm 14.54
Male, n (%)	7 (35.0)	26 (46.4)
DTaP vaccination, n (%)	20 (100.0)	Unknown
Tdap vaccination, n (%)	0 (0.0)	0 (0.0)
Cough duration, mean \pm SD (days)*	11.35 \pm 3.33	18.43 \pm 4.04
ELISA GMT, mean \pm SD (EU/mL) [†]	57.35 \pm 1.77	55.54 \pm 1.93

* $P < 0.001$; [†] $P = 0.004$.

against pertussis or determination of infection status through the measurement of pertussis antibodies. The most reliable antibody test known up to present is confirmation of at least a 4-fold increase in antibody titers pre- and post-vaccination or infection with pertussis (13). In this point of view, our study has a limitation in that the majority of pertussis cases were diagnosed based on one measurement of antibody titer, even though 3 cases were diagnosed with culture and 10 cases were detected with PCR.

Studies in adolescents and adults with persistent cough have been reported in Korea and other countries (2, 9, 14, 15). Although these studies indicated different results depending on the time of study and diagnostic method used, they indicated that a high percentage of adolescents and adults with persistent cough (up to 40.0%) developed the symptom due to pertussis. In this study, pertussis was positive in 24.5% of adolescents and adults with persistent cough in Korea. To our knowledge, it is the highest rate amongst the pertussis epidemiology studies conducted in Korean population.

The study results suggest the importance of adequate management of adolescents and adults with persistent cough in order to address the recent trend of increasing incidences of pertussis again in Korea. Particularly, if adolescents and adults are affected with pertussis, unlike during infancy, they may show atypical symptoms (13, 15). Considering this aspect, the actual proportion of Korean adolescents and adults with chronic cough that is attributable to pertussis could be even higher than that indicated in the study results. Therefore, it is necessary to actively diagnose and treat pertussis, taking into account that persistent cough can possibly be caused by pertussis in Korean adolescents and adults.

DISCLOSURE

The authors have no conflicts of interest to disclose.

AUTHOR CONTRIBUTION

Design of the study: Kang JH. Data and samples collection: Lee SY, Han SB, Kim JS. Writing manuscript: Lee SY, Kang JH. Revision: Lee SY. Manuscript approval: all authors.

ORCID

Soo Young Lee <http://orcid.org/0000-0002-5354-3135>

Seung Beom Han <http://orcid.org/0000-0002-1299-2137>

Jin Han Kang <http://orcid.org/0000-0003-1610-6742>

Ju Sang Kim <http://orcid.org/0000-0003-3937-3181>

REFERENCES

1. Lee SY, Kim JS, Ahn JH, Choi JH, Ma SH, Park JS, Kim HM, Kang JH. *Immunoassay of diphtheria and tetanus according to ages. Infect Chemother* 2012; 44: 62-6.
2. Lee SY, Choi UY, Kim JS, Ahn JH, Choi JH, Ma SH, Park JS, Kim HM, Kang JH. *Immunoassay of pertussis according to ages. Korean J Pediatr Infect Dis* 2012; 19: 55-60.
3. Korea Centers for Disease Control and Prevention. *Communicable diseases surveillance yearbook, 2008. Seoul, Republic of Korea: Korea Centers for Disease Control and Prevention* 2009.
4. Korea Centers for Disease Control and Prevention. *Infectious diseases surveillance yearbook, 2011. Seoul, Republic of Korea: Korea Centers for Disease Control and Prevention, 2012.*
5. Wendelboe AM, Van Rie A, Salmaso S, Englund JA. *Duration of immunity against pertussis after natural infection or vaccination. Pediatr Infect Dis J* 2005; 24: S58-61.
6. Plotkin SA. *Immunologic correlates of protection induced by vaccination. Pediatr Infect Dis J* 2001; 20: 63-75.
7. Choi KM, Kim KH, Kim YJ, Kim JH, Park SE, Lee HJ, Eun BW, Jo DS, Choi EH, Hong YJ. *Recommendation for the use of newly introduced Tdap vaccine in Korea. Korean J Pediatr* 2011; 54: 141-5.
8. Senzilet LD, Halperin SA, Spika JS, Alagaratnam M, Morris A, Smith B; Sentinel Health Unit Surveillance System Pertussis Working Group. *Pertussis is a frequent cause of prolonged cough illness in adults and adolescents. Clin Infect Dis* 2001; 32: 1691-7.
9. Park WB, Park SW, Kim HB, Kim EC, Oh M, Choe KW. *Pertussis in adults with persistent cough in South Korea. Eur J Clin Microbiol Infect Dis* 2005; 24: 156-8.
10. Kwon HJ, Yum SK, Choi UY, Lee SY, Kim JH, Kang JH. *Infant pertussis and household transmission in Korea. J Korean Med Sci* 2012; 27: 1547-51.
11. Reizenstein E, Hallander HO, Blackwelder WC, Kühn I, Ljungman M, Möllby R. *Comparison of five calculation modes for antibody ELISA procedures using pertussis serology as a model. J Immunol Methods* 1995; 183: 279-90.
12. Greco D, Salmaso S, Mastrantonio P, Giuliano M, Tozzi AE, Anemona A, Ciofi degli Atti ML, Giammanco A, Panei P, Blackwelder WC, et al. *A controlled trial of two acellular vaccines and one whole-cell vaccine against pertussis. Progetto Pertosse Working Group. N Engl J Med* 1996; 334: 341-8.
13. Cherry JD, Grimprel E, Guiso N, Heininger U, Mertsola J. *Defining pertussis epidemiology: clinical, microbiologic and serologic perspectives. Pediatr Infect Dis J* 2005; 24: S25-34.
14. Cornia PB, Hersh AL, Lipsky BA, Newman TB, Gonzales R. *Does this coughing adolescent or adult patient have pertussis? JAMA* 2010; 304: 890-6.
15. Rendi-Wagner P, Tobias J, Moerman L, Goren S, Bassal R, Green M, Cohen D. *The seroepidemiology of Bordetella pertussis in Israel: estimate of incidence of infection. Vaccine* 2010; 28: 3285-90.