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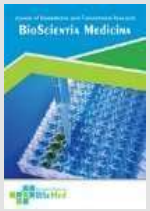

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Differences in Mean Anti-Pertussis Antibody Levels in Children with Acellular Pertussis Immunization and Whole Pertussis Without Booster

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A B S T R A C T

Background: The incidence of pertussis is increasing every year, especially in developing countries. Low immunization coverage and decreased immunity are some of the factors causing the re-increase in pertussis cases. The protection provided by the pertussis vaccine whole and acellular pertussis given as a baby will decrease with age. This study aims to determine the difference in mean levels of anti-pertussis antibodies in children who received acellular pertussis and whole pertussis immunization without a booster. **Methods:** A cross-sectional study was carried out at the pediatric polyclinic of Dr. M. Djamil General Hospital Padang from December 2022 to December 2023. Research subjects were children aged 5-9 years with a history of whole pertussis immunization (DPwT) 3 times or acellular pertussis immunization (DPaT) 3 times. The research subjects were examined for anti-pertussis antibody titers using the ELISA technique. **Results:** Thirty-four children with a history of DPwT immunization 3 times and 34 children with a history of DPwT immunization 3 times were research subjects, with mean age 6.94±1.49 in the DPwT group and 6.88 ±1.61 in the DPaT group. The mean anti-pertussis antibody level in the DPwT group (9.54 IU/mL) was higher than the DPaT group (6.96 IU/mL) but was not statistically significant ($p>0.05$). The average antibody results showed that the antibody levels in both groups were below the antibody titer threshold that provides protection against pertussis. The results of the analysis showed that there was a significant difference in the incidence of AEFI between the DPwT and DPaT immunization groups ($p<0.05$). **Conclusion:** There was no difference in anti-pertussis antibody levels in children who received DPwT and DPaT immunization 3 times. Pertussis immunization is a required booster so that antibody levels are sufficient to provide protection against pertussis.

1. Introduction

Pertussis, or whooping cough, is a highly contagious respiratory disease caused by *Bordetella pertussis* bacteria. The disease is characterized by a persistent, severe cough, often accompanied by a "whooping" sound when inhaling. Pertussis can be fatal in infants and young children and is one of the main causes of child death in developing countries. The incidence of pertussis is increasing every year, especially in developing countries. In many developing countries, immunization coverage for pertussis remains below the targets recommended by the World Health Organization (WHO). This causes many children who are not protected from this disease. Immunity to pertussis obtained from vaccination will decrease over time. This means that children vaccinated as babies may no longer be protected against the disease several years later. New strains of pertussis bacteria that are more resistant to antibiotics have emerged in recent years. This makes treating pertussis more difficult and increases the risk of complications. The increasing movement of people

between countries makes it easier for infectious diseases such as pertussis to spread.[1-3]

Vaccination is one of the most effective ways to prevent pertussis. Pertussis vaccine is available in two main types, namely whole (DPwT) and acellular (DPaT). Each type has its own advantages and disadvantages. The whole pertussis vaccine contains killed pertussis bacteria cells. This vaccine has been used since the 1920s and is very effective in preventing severe pertussis. The advantage of the DPwT vaccine is that it is very effective in preventing severe pertussis and protecting against atypical pertussis infections. Meanwhile, the disadvantage of the DPwT vaccine is that it more often causes side effects, such as fever, redness, and pain at the injection site. These side effects are usually mild and disappear within a few days. It is not recommended for girls aged 13-18 years and pregnant women because of the risk of side effects. the more serious side. The acellular pertussis vaccine only contains several components of the pertussis bacteria, namely toxins and hemagglutination filaments. This vaccine causes fewer side effects than the whole vaccine but is also less effective in preventing severe pertussis. The advantages of the DPaT vaccine are that it rarely causes side effects, and is safe for girls aged 13-18 years and pregnant women. Meanwhile, the drawback of the DPaT vaccine is that it is less effective in preventing severe pertussis and does not protect against atypical pertussis infections.[4-8] This study aims to determine the difference in mean levels of anti-pertussis antibodies in children who received acellular pertussis immunization and whole pertussis immunization without a booster. This study is very important because it can provide information about the long-term effectiveness of whole and acellular pertussis vaccines. This information can be used to help develop more effective pertussis immunization programs in the future.

2. Methods

The study design uses an observational analytical research design with a cross-sectional study type. This research was conducted at the pediatric polyclinic of Dr. M. Djamil General Hospital Padang from December 2022 to December 2023. A total of 68 research subjects participated in this study, where the research subjects met the inclusion criteria. The inclusion criteria in this study were children aged 5-9 years, who had received pertussis immunization 3 times and had a KIA book or had a record of administering the DPaT vaccine 3 times or had a record of administering the DPwT vaccine 3 times. Meanwhile, the exclusion criteria were that parents did not agree and were unwilling to take part in the research by signing informed consent, received pertussis infection or pertussis vaccine in the last 1 year, received acellular and whole pertussis immunization in 3 administrations (mixed), suffered from malignancies, immunodeficiency diseases, and hematological disorders requiring serial blood transfusions. The sampling technique was carried out by consecutive sampling. This research was carried out after receiving informed consent from the child's parents and has received research ethics approval from the research and health ethics committee of Dr. M. Djamil General Hospital Padang number LB.02.02/5.7/406/2023.

Children who met the inclusion criteria and did not meet the exclusion criteria were taken as research samples, data were recorded, namely name, age, gender, weight and height, parents' education level, age at first pertussis vaccine, history of pertussis infection, immunization data pertussis, and post-immunization adverse events and consent as a research subject with proof of a consent form signed by the parents. A blood sample was taken via venipuncture of 2 ml which was inserted into a tube vacutainer, samples were transported using a cooler box to the Biomedical Laboratory, Faculty of Medicine, Universitas Andalas. The samples were centrifuged and then stored at a cooler temperature of 2-8°C. Samples were examined in the Biomedical Laboratory, Faculty of Medicine, Universitas Andalas using the ELISA method using *B. pertussis* toxin (PT) kit IgG NovaLisa made by PT NovaTec with product number

BPTG0610. Univariate analysis was carried out to describe each variable studied. Normal distribution numerical data is presented in the form of mean ± standard deviation (SD). Numerical data does not have a normal distribution so it is presented in the form of median, minimum, and maximum. Categorical data is presented in the form of frequencies and percentages for each category. Bivariate analysis began by using a data normality test using the Shapiro-Wilk test (n < 50). In examining the difference in mean levels of anti-pertussis antibody titers in children who received acellular pertussis and pertussis vaccines whole analysis is used T-test.

3. Results

Table 1 shows that there are no differences in gender, child's age, father's age, father's education, mother's age, mother's education, age, receiving the last pertussis vaccine, history of pertussis, AEFI with reddish and fussy skin and nutritional status in children aged 5- 9 years old with a history of DPwT or DPaT immunization (p>0.05). However, there is a difference in AEFI fever in children aged 5-9 years with a history of DPwT or DPaT immunization (p<0.05), where it occurs more often in children with a history of DPwT (91.2%) than DPaT (35.3%).

Table 1. Characteristics of respondents.

Category	wP	aP	p-value
Child's gender, f (%)			0,464
Male	13 (38,2)	17 (50,0)	
Female	21 (61,8)	17 (50,0)	
Child's age, (mean±SD)	6,94±1,49	6,88±1,61	0,876
Father's age (years), (mean±SD)	40,00±7,34	37,62±5,02	0,123
Father's education level, f (%)			
Primary school	2 (5,9)	1 (2,9)	
Junior high school	6 (17,6)	3 (8,8)	
Senior high school	20 (58,8)	12 (35,3)	
Diploma	3 (8,8)	4 (11,8)	
Bachelor's degree	3 (8,8)	10 (29,4)	
Master's degree	0	4 (11,8)	
Maternal age (years), (mean±SD)	35,91±6,49	35,06±4,63	0,624
Mother's education level, f (%)			0,453
Junior high school	5 (14,7)	2 (5,9)	
Senior high school	18 (52,9)	16 (47,1)	
Diploma	6 (17,6)	7 (20,6)	
Bachelor's degree	5 (14,7)	9 (26,5)	
Master's degree			
Age received last pertussis vaccine (months), (mean ± SD)	5,88±1,20	5,91±0,87	0,908
History of pertussis, f (%)	0	0	n/a
KIPI, f (%)			
Fever	31 (91,2)	12 (35,3)	<0,001*
Reddish skin	1 (2,9)	0	1,000
Fussy	6 (17,6)	5 (14,7)	1,000
Seizures	0	1 (2,9)	1,000
Nutritional status			0.580
Poor nutrition	0	0	
Malnutrition	14 (41,2)	8 (23,5)	
Good nutrition	20 (58,8)	24 (70,6)	
Overweight	0	2 (5,9)	
Obesity	0	0	

*P<0.05 significant; n/a, not account.

Table 2 shows that the anti-pertussis antibody level of the DPwT vaccine is 9.54 IU/mL, which is higher than DPaT, namely 6.96 IU/mL. Based on the results of the analysis, it is known that there is no difference between the levels of anti-pertussis antibody titers in children who received acellular pertussis vaccine and whole pertussis (p > 0.05).

Table 2. Differences in mean levels of anti-pertussis antibody titers in children who received acellular pertussis and whole pertussis vaccines.

Variable	wP median (min-maks)	aP median (min-maks)	p-value
Anti-pertussis antibody titer (IU/mL)	9,54 (0,34-131,49)	6,96 (0,38-151,65)	0,704*

p*<0.005 significant; Mean-Whitney test.

Table 3 shows that antibody titers ≥24 IU/mL were more common in children who received acellular pertussis vaccine (32.4%) than whole pertussis (17.6%). Based on the results of statistical tests using chi-square, it is known that there is no relationship between anti-pertussis antibody titers in children who received acellular pertussis and pertussis vaccines whole (p>0,05).

Table 3. Chi-Square test relationship between anti-pertussis antibody titers in children who received acellular pertussis and whole pertussis vaccines.

Vaccine	Antibody titer (f/%)		p-value
	<24 IU/mL	≥24 IU/mL	
aP	23 (67,6)	11 (32,4)	0,263
wP	28 (82,4)	6 (17,6)	
Total	51 (75,0)	17 (25,0)	

4. Discussion

The results of examining anti-pertussis antibody levels in the two groups showed median results that were not much different, namely 9.54 IU/mL in children with a history of DPwT immunization and 6.96 IU/mL in children with a history of DPaT immunization. Although the median in the group that received whole pertussis immunization was higher than the acellular group, this difference was not statistically significant. Antibody levels in the two groups were not much different and were not statistically significant because basically, the acellular pertussis vaccine used had almost the same efficacy as whole pertussis, although this efficacy value differs in several studies. International standards are applied so that existing vaccines have the same safety. Various efforts are made to increase vaccine safety, reduce adverse reactions, and increase the vaccine's protective power. Twelve of the 34 children (35%) who received acellular pertussis immunization had antibody titer levels below the protection threshold, namely≤ 24 IU/mL and there was 1 child with an antibody titer indicating an infection that occurred in the last 1 year, namely≥ 100 IU/mL. In the group of children who received whole pertussis immunization, there were 5 out of 34 children (14%) with antibody levels that provided protection. Extreme values were obtained in both groups, where antibody levels increased 3 times the median value. Extreme values in the sample can be suspected due to a pertussis infection that occurred in the last 1 year which was not diagnosed and the history of the diagnosis of pertussis infection was obtained from interviews with parents, so the information obtained is likely to be inaccurate.

Statistical research results showed that the average anti-pertussis antibody levels in both groups were still below the levels that could provide

protection. This is reasonable because all research subjects did not receive the DPT vaccine booster. The clinical aspect of the results of this research is how important it is for booster vaccines to be given to children in an effort to maintain antibodies at levels that can provide protection against pertussis because antibody levels will decrease as age increases.[9-14]

The results of the study showed that there were more subjects in the DPaT vaccine group with antibody titer levels ≥24 IU/mL than in the DPwT vaccine group, although this result was not statistically significant. Only 25% of all samples from both groups had antibody results that were considered to provide protective value. This result is different from previous research which found a greater reduction in antibody levels when administering acellular vaccines compared to whole. Based on these results, it can be seen that there is a decrease in pertussis antibody levels with a distance of more than 5 years from the last immunization. Previous research in several countries also concluded that there was a reduction in pertussis antibody levels of more than 50% in children who received their last immunization more than 4 years ago. The latest meta-analysis study concludes that the pertussis vaccine can only provide protection for 3 years, so a vaccine is needed booster to increase the level of anti-pertussis antibodies in the blood again. Similar results were also obtained from other research which found a decrease in anti-pertussis levels in research subjects who had received DPT vaccination 3 times. The results of this study cannot explain whether anti-pertussis was formed in the subjects and then decreased or whether it was not formed from the start because there was no initial data. Antipertussis antibody levels ranged from 0.338 IU/mL to 151.65 IU/mL. The range of antibody levels in the two groups was found to be very wide, causing the distribution to be abnormal, so the median value was used in this study. The difficulty faced in this research was that not many parents still kept immunization records even though the parents were quite sure that their children had received DPT immunization 3 times and were willing to take part in the research. Generally, this is because the healthy card (KMS) book you own is not kept by yourself but is kept at the Integrated Services Post and its whereabouts are difficult to trace. Possession of immunization records was included in the inclusion criteria to prevent the occurrence of recall bias. Immunization records should also include the interval between immunizations as one of the factors that determine the immune effectiveness of a vaccine. In the future, this vaccine administration interval can be used as a data entry for the characteristics of research subjects which also influences anti-pertussis antibody titer levels.[15-20]

Another limitation of this study is that the measurement of anti-pertussis antibody levels was only carried out once with a cross-sectional design so that anti-pertussis antibody levels could not be seen clearly. The level of anti-pertussis antibodies after basic DPT vaccination is unknown so no preliminary data on the subject's anti-pertussis antibody levels was obtained as an indication of whether or not anti-pertussis antibodies were formed after vaccination. It is hoped that in the future a study can be carried out with a cohort design that can measure anti-pertussis antibody levels after vaccination and 5-6 years after the last vaccination to get ideal results. Another limitation is that the ELISA method used in this study cannot differentiate whether anti-pertussis antibodies can be caused by vaccination or due to natural infection. It is necessary to clearly record the diagnosis of pertussis infection in children to avoid extreme values that can occur.[21,22]

5. Conclusion

There was no difference between anti-pertussis antibody titer levels in children who received acellular pertussis and whole pertussis vaccines.

6. References

1. Licona D, Delgado-Jesus. Mortality in pertussis Mexico 2022. Bol Clin Hosp Infant Edo Son. 2022; 35: 1–10.

2. Tjahjowargo S, Gunardi H. Evidence-based case report comparing the effectiveness and safety of acellular and whole-cell. Sari Pediatrics. 2017;1 8(5): 403-8
3. Alghounaim M, Alsaffar Z, Alfraij A, Bin-Hasan S, Hussain E. Whole-cell and acellular pertussis vaccine: reflections on efficacy. Med Princ Prac. 2022; 31: 313–21.
4. Paradowska-Stankiewicz I, Rumik A, Bogusz J, Zbrzeźniak J, Rastawicki W, Śmietańska K, et al. Duration of protection against *Bordetella pertussis* infection elicited by whole-cell and acellular vaccine priming in Polish children and adolescents. Vaccine. 2021; 39: 6067–73.
5. Gao H, Lau EHY, Cowling BJ. Waning immunity after receipt of pertussis, diphtheria, tetanus, and polio-related vaccines: a systematic review and meta-analysis. Journal of Infectious Diseases. Oxford University Press; 2022; 225: 557–66.
6. Sunarno S, Sofiah SN, Amalia N, Hartoyo Y, Rizki A, Puspandari N, et al. Laboratory and epidemiology data of pertussis cases and close contacts: a 5-year case-based surveillance of pertussis in Indonesia, 2016–2020. PLoS One. 2022; 17: 0266033.
7. Yeshanew AG, Lankir D, Wondimu J, Solomon S. Pertussis outbreak investigation in Northwest Ethiopia: a community based study. PLoS One. 2022; 1
8. Jayasundara D, Randall D, Sheridan S, Sheppeard V, Liu B, Richmond PC, et al. Estimating the excess burden of pertussis disease in Australia within the first year of life, that might have been prevented through timely vaccination. Int J Epidemiol. 2023; 52(1): 250-9
9. Alghounaim M, Alsaffar Z, Alfraij A, Bin-Hasan S, Hussain E. Whole cell and acellular pertussis vaccine: reflections on efficacy. medical principles and practice. International Journal of the Kuwait University, Health Science Centre. NLM (Medline). 2022; 31: 313–21.
10. Tessier E, Campbell H, Ribeiro S, Rai Y, Burton S, Roy P, et al. Impact of the COVID-19 pandemic on *Bordetella pertussis* infections in England. BMC Public Health. 2022; 22.
11. Setiawan MS, Wijayanto AW. Determinants of immunization status of children under two years old in Sumatera, Indonesia: a multilevel analysis of the 2020 Indonesia national socio-economic survey. Vaccine. 2022; 40: 1821–8.
12. Gabutti G, Cetin I, Conversano M, Costantino C, Durando P, Giuffrida S. Experts' opinion for improving pertussis vaccination rates in adolescents and adults: a call to action. Int Jo Environ Res Public Health. MDPI. 2022; 19
13. Zerbo O, Fireman B, Klein NP. Lessons from a mature acellular pertussis vaccination program and strategies to overcome suboptimal vaccine effectiveness. Expert Rev Vaccines. 2022; 21: 899–907.
14. Abu-Raya B, Esser MJ, Nakabembe E, Reiné J, Amaral K, Diks AM, et al. Antibody and B-cell immune responses against *Bordetella pertussis* following infection and immunization. J Mol Biol. 2023; 435: 168-74.
15. Klimova N, Holubova J, Streparola G, Tomala J, Brazdilova L, Stanek O, et al. Pertussis toxin suppresses dendritic cell-mediated delivery of B. pertussis into lung-draining lymph nodes. PLoS Pathog. 2022; 18.
16. Versteegen P, Bonačić Marinović AA, van Gageldonk PGM, van der Lee S, Hendrikx LH, Sanders EAM, et al. Long-term immunogenicity upon pertussis booster vaccination in young adults and children in relation to priming vaccinations in infancy. Vaccines Basel. 2022; 10.
17. Silva RP, DiVenere AM, Amengor D, Maynard JA. Antibodies binding diverse pertactin epitopes protect mice from Bordetella pertussis infection. J Biol Chem. 2022; 298.

18. Gao H, Lau EHY, Cowling BJ. Waning immunity after receipt of pertussis, diphtheria, tetanus, and polio-related vaccines: a systematic review and meta-analysis. J Infect Dis. Oxford University Press. 2022; 225: 557–66.
19. Tripathy SK, Das S, Malik A. Vaccine and malnutrition: a narrative review. J Family Med Prim Care. 2023; 12: 1808–13.
20. Gonzales A, Choque D, Marcos-Carbajal P, Salvatierra G. Factors associated with diphtheria vaccination completion among children under five years old in Peru 2010–2019: a cross-sectional population-based study. Heliyon. 2022; 8.
21. Diks AM, Versteegen P, Teodosio C, Greenland RJ, de Mooij B, Buisman AM, et al. Influence of age and primary vaccination background on the plasma cell response to pertussis booster vaccination. Vaccines (Basel). 2022; 10.
22. Seppälä E, Kristoffersen AB, Bøås H, Vestrheim DF, Greve-Isdahl M, De Blasio BF, et al. Pertussis epidemiology including direct and indirect effects of the childhood pertussis booster vaccinations, Norway, 1998–2019. Vaccine. 2022; 40: 3142–9.