

One Year Antibody After Vaccination Human Papilloma Virus of Children in Elementary School of Cipayang Subdistrict, East Jakarta, Jakarta, Indonesia

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Received: 12 April 2020; Accepted: 01 May 2020

Citation: Cicilia Windiyaningsih, Dian Ratnamurti. One Year Antibody After Vaccination Human Papilloma Virus of Children in Elementary School of Cipayang Subdistrict, East Jakarta, Jakarta, Indonesia. *Microbiol Infect Dis*. 2020; 4(2): 1-5.

ABSTRACT

Every woman is at risk of infection the Human Papilloma Virus that causes Cervical Cancer, in Indonesia there were estimated to be $\pm 100,000$ new cervical cancers every year and every hour a woman dies from cervical cancer. DKI Jakarta has cervical cancer rate of 1.2 / 1000 women.

Purpose: This research was to prove the antibodies one year after being vaccinated with Human Papilloma Virus in elementary school children in the working area of the Cipayang District Public Health Center, East Jakarta.

Applied research: Intervention studies in all girls in grade VI elementary school and population of elementary school girl in DKI Jakarta amounted to 750,000. Samples of 44 respondents were taken by random sampling, direct interviews with questionnaires.

Results: Antibody levels were positive for Human papilloma virus 9 children (20.5%), age 11 years 50%, 12-14 years 50%, normal nutritional status 68.2%, genetic cancer 11.4% mothers, fathers 9.1%, grandfather 2.3%, grandmothers 6.8%, younger sisters 9.1%, sister 9.1%; follow-up events after vaccination were fever 11.4%, positive undurability 9.1%, itching 90.9%, positive stiffness 29.5%, pain 11.4%, swelling 15.9%, dizziness 9.1%, nausea 9.1%. The results of antibody associations with 18 variables that were significant only 9 variables such as unduration, fever, itching, pain, nausea, dizziness, genetic mother, father, grandfather, sister, while the rest of it p value > 0.05 .

Conclusion: Antibody positive 20.5%, the rest have not formed antibodies.

Keywords

Antibodies, HPV vaccination, Elementary school girls.

Introduction

Cervical cancer is one of the problems in reproductive health. Cervical cancer is a malignancy that occurs in the cervix. In 2012, there were 528,000 new cases of cervical cancer, which have been diagnosed worldwide and 85% occur in less developed areas. Cervical cancer causes 266,000 women to die of cervical cancer each year. Cervical cancer represents 7.5% of deaths from all deaths caused by cancer in women [1]. Every woman is at risk of contracting the Human Papilloma Virus that causes Cervical Cancer, in Indonesia there are estimated to be $\pm 100,000$ new

cervical cancers every year and every hour a woman dies from cervical cancer. Since 2000-2012 the age of women with cervical cancer is getting younger, which is the age range of 21-22 years. According Ministry of Health Information Data Center R.I. 2015. In Indonesia, 34 provinces were diagnosed with the highest cervical cancer sufferers in Yogyakarta with 1.5 / 1000 female cervical cancer sufferers, North Maluku (1.5 / 1000), North Sulawesi (1.4 / 1000), Papua (1, 3/1000), DKI Jakarta cervical cancer morbidity rate is 1.2 / 1000 women. (Information Center Data Ministry of Health R.I. in 2015) [2].

Based on information from the DKI Jakarta Provincial Health Office, HPP mass vaccinations have been carried out for grade V

and VI elementary school children in the Jakarta Region, including East Jakarta, Cipayang District. After the HPV vaccination of these elementary school girls, there has not been an evaluation of antibodies and subsequent events after vaccination.

Research Objective

Proving antibodies one year after being given human papilloma virus (Gardasil) vaccination to elementary school girls in the working area of the Cipayang District Health Center, East Jakarta, DKI Jakarta, Indonesia.

Research Method

Applied research methods with intervention design. The study population was all girls in grade VI elementary school and equivalent in DKI Jakarta totaling 750,000. A sample of 44 respondents was taken by random sampling, data collection using data from medical records and direct interviews using standardized questionnaires. Blood taken from cubital veins as much as 3 cc with venoject (venotube + needle) and holder, then centrifuged with 1500 RPM to get serum after taking venous blood cubiti was given antiseptic and sterile hansaplast to avoid infection, then examined with ELISA to see antibody levels the positive. Analysis of research data in descriptive and non-parametric analytic chi square. The vaccine used for the quadrivalent 40 µg vaccination of HPV 11 L1 HPV protein (GARDASIL produced by Merck) L1 protein from VLP HPV type 6/11/16/18 is expressed through a recombinant *Saccharomyces cerevisiae* (yeast) vector. Each 0.5 cc contains 20µg of 6 L1 HPV protein, 40 µg of 11 L1 HPV protein, 20 µg of HPV18 L1 protein. Each 0.5 ml contains 225 amorph aluminum hydroxyphosphatase sulfate. The formula also contains sodium borate. This vaccine does not contain timerasol and antibiotics. This vaccine should be stored at 2°C-8°C. The vaccine is given 0.5 cc Intramuscular, serology examined one year after vaccination. Antibody testing with ELISA. Descriptive and non-parametric analysis with Chi Square. Ethical clearance was approved, no conflict of interested.

Research Results

The report on the HPV vaccination results of the Cipayang District

Health Center in 2017 shows the HPV coverage data from 10 villages that have been given HPV vaccination in primary V grade children by 99% and grade 6 by 100%.

Descriptive Analysis

No	Variable	Result	
1	Age	11 year	22 50%
		12- 14 year	22 50%
2	Nutritional Cases	Not Normal	14 31.8
3	Cancer History	Mother	5 11.4
		Father	4 9.1
		Grandfather	1 2.3
		Grandmother	3 6.8
		Older Brother/Sister	4 9.1
		Younger Brother/Sister	4 9.1
4	Side Effect after HPV Vaccination	Fever	5 11.4
		Rash	4 9.1
		Ache	13 29.5
		Pain	5 11.4
		Swollen	7 15.9
		Dizziness	4 9.1
		Nausea	4 9.1
		Positive Induration	4 9.1
5	Positive Antibody	9 20.5	

Table 1: Respondent Distribution Based on Characteristic, Genetic, Side Effect after Vaccination and Elementary School Children Antibody In Cipayang Public Health Centre.

Based on descriptive analysis describing respondents who experienced a follow-up event after HPV vaccination in school children were 15 people (34.1%), while there were 4 children who experienced 8 follow-up events after vaccination mentioned above, who experienced 1 incident totaling 9 children, and 2 and 3 occurrences of 1 child each. Children aged 11 years are 50%, 12-14 years are also 50%, and genetically have a family history of cancer in 11.4% (5 children). Normal nutritional status is 68.2%. Positive antibodies after vaccination are 20.5%.

NO	Variable	Antibody				p value	OR (95% CI)	
		Positive		Negative				
		n	%	n	%			
1	Age	11 year	6	67.3	16	45.7	0.162	2.375 (0,511-11.047)
		12-14 year	3	32.7	19	44.3		
2	Nutritional Status	Normal	5	55.6%	9	25.7%	0,077	0.277 (0.065-1.263)
		Not Normal	4	44.4%	26	74.3%		
3	Cancer in Mother	Positive	3	33.3%	2	5.7%	0,046	8.250 (1.128-60.319)
		Negative	6	66.7%	33	94.7%		
4	Cancer in Father	Positive	3	33.3%	1	2.9%	0,022	17.000 (1.506-191.922)
		Negative	6	66.7%	34	97.1%		
5	Cancer in Grandmother	Positive	2	22.2%	1	2.9%	0,095	9.714 (0.770-122.505)
		Negative	7	77.8%	34	97.1%		

6	Cancer in Grandfather	Positive	3	33.3%	1	2.9%	0,022	17.000 (1.506-191.922)
		Negative	6	66.7%	34	97.1%		
7	Cancer in Older Brother/Sister	Positive	1	11.1%	0	0.0%	0,205	0.186 (0.100-0.348)
		Negative	8	88.9%	35	100.0%		
8	Breast Cancer	Positive	1	11.1%	1	2.9%	0,330	4.250 (0.239-75.470)
		Negative	8	44.4%	34	97.1%		

Table 2: Analysis of the Relationship between Antibodies and Age Factors, Nutritional Status and Genetic Cancer in Elementary School Girls in the Cipayang Community Health Center, East Jakarta, Indonesia Year 2019.

NO	Variable		Antibody				p value	OR (95% CI)
			Positive		Negative			
			n	%	n	%		
1	Fever	Positive	3	33.3	2	5.7	0.046	8.250 (1.128-60.319)
		Negative	6	66.7	33	94.3		
2	Rash	Positive	3	33.3	1	2.9	0.022	17.000 (1.506-191.922)
		Negative	6	66.7	34	97.1		
3	Ache	Positive	3	33.3	10	28.6	0.297	1.250 (0,261-5.996)
		Negative	6	66.7	25	71.4		
4	Pain	Positive	3	33.3	2	5.7	0.022	17.000 (1.506-191.922)
		Negative	6	66.7	33	94.3		
5	Swollen	Positive	3	33.3	4	11.4	0.162	2.375 (0,511-11.047)
		Negative	6	66.7	31	88.6		
6	Unduration	Positive	3	33.3	1	2.9	0.022	17.000 (1.506-191.922)
		Negative	6	66.7	34	97.1		

Table 3: Analysis of the Relationship Between Antibodies and Side Effect Factor of Post-HPV Vaccination in Elementary School Girls in the Cipayang Community Health Center, East Jakarta, Jakarta, Indonesia in 2019.

Based on table 2 There was genetically significant correlation with cancer in mothers, fathers and grandparents with p value < 0.05, while the nutritional factors, and age had not significant relationship.

Base on table 3 the results of Chi square analysis of variables associated with positive antibodies with Side effect events after HPV vaccination with p <0.05 are fever, itching, pain and induration, dizziness, nausea. Whereas the variables whose p value > 0.05 are swollen, ache.

Induration	p Value	OR (95%CI)	R Square Nagel Kerke
Positive	0.038	8.250 (1.128-60.319)	14.8%
Negative			

Table 4: Regression Logistic Analysis Result.

Table 4 in the multiple logistic regression analysis, only one variable affected HPV vaccination, namely unduration at the time of vaccination with a contribution of 14.8%.

Discussion

HPV Antibodies

The results of this study were positive antibodies after being given an HPV vaccine of 20.45%, probably because they had just received a dose of the HPV vaccine, while other studies on a review of the literature by Jade Pattyn, Severien Van Keera,

Wiebren Tjalmab, Veerle Matheussen, Pierre Van Dammea, Alex Vorstersa from journal homepage: www.elsevier.com/locate/pvr [3]. The systematic search and selection process yielded 44 articles with title infection and vaccine-induced HPV-specific antibodies in cervico vaginal secretions was the evidence of HPV-specific antibodies in CVS after natural infection (26/44) and HPV vaccination (18/44) is discussed [3]. Many studies indicate that HPV specific antibody detection in CVS is variable but feasible with a variety of collection methods and immunoassays. Most CVS samples were collected by cervico vaginal washing or wicks, and antibody presence was mostly determined by VLP-based ELISAs. The moderate to strong correlation between vaccine-induced antibody levels in serum and in CVS indicates that HPV vaccines generate antibodies that transudate through the cervical mucosal epithelium. Human papillomavirus vaccination induces neutralizing antibodies in oral mucosal fluids by A Handisurya, C Schellenbacher, A Haitel, T Senger and R Kimbauer, Department of Dermatology, Medical University of Vienna, Waehringer Guertel 18-20, A-1090 Vienna, Austria; and Department of Pathology, Medical University of Vienna, Waehringer Guertel 18-20, A-1090 Vienna, Austria and Department of Genome Modifications and Carcinogenesis, German Cancer Research Center, 69120 Heidelberg, Germany [4]. HPV-vaccination induced type-specific antibodies in sera and oral fluids of the vaccines. Importantly, the antibodies in oral fluids were capable of neutralizing HPV pseudovirions in vitro, indicating protection from infection. The

increased neutralizing antibody levels against HPV16/18 in sera and oral fluids post-vaccination correlated significantly within an individual. Conclusions: We provide experimental proof that HPV-vaccination elicits neutralizing antibodies to the vaccine-targeted types in oral fluids. Hence, immunization may confer direct protection against type-specific HPV infection and associated diseases of the oropharyngeal tract. Measurement of antibodies in oral fluids represents a suitable tool to assess vaccine-induced protection within the mucosal milieu of the oropharynx.

In a study conducted by Dewi Setiawati (2014), it was found that the bivalent HPV 16/18 VLP vaccine was very effective in reducing the incidence of HPV infection and 16/18 HPV permanent infection in individuals who had received complete HPV vaccinations in young women [5].

Persistent human papillomavirus (HPV) infection is associated with cervical cancer and other HPV-related diseases and tumors. Thus, characterization of the long-term immunity to the currently available HPV vaccine is important. A total of 149 female subjects vaccinated with Cervarix or Gardasil participated in this study and they were grouped by age (10-12 years) and aged 16-20 years). Humoral immune responses (IgG and neutralizing antibody titers, antibody avidity) and circulating memory B cells were analyzed after a mean of 4-6 years from the third immunization. Humoral responses to HPV-16 and HPV-18 (and HPV-6 and HPV-11 for Gardasil) are high in the age group and vaccines for up to six years from the third dose. However, Cervarix induces a higher and more persistent antibody response, while Cervarix two vaccines are somewhat equivalent in inducing memory B cells against HPV-16 and HPV-18. In addition, the percentage of subjects with vaccine-specific memory B cells was even superior to the Gardasil vaccine and, conversely, Cervarix vaccinated individuals with circulating antibodies, but undetectable memory B cells were found. Finally, a higher proportion of Cervarix vaccine subjects showed a cross-neutralization response to the non-vaccine types of HPV-31 and HPV-45. Gardasil and Cervarix can, thus, differently affect long-lasting humoral immunity from both quantitative and qualitative perspectives.

Post-HPV Vaccination Incidence and Its Impact on the formation of antibodies

Respondents for children aged 11 years are 50%, 12 years are 45.45% and the rest are aged 14 years 4.5%. The most common post-vaccination events that occurred in children after HPV vaccination were 13 children (29.5%), 7 children (15.9%) swelling, 5 children (11.4%) fever, and 5 children pain (11.4%). The results of this study are in line with Dewi Setiawati (2014) explaining that reactions due to vaccination can cause interference at the injection site, in the form of pain, redness, and swelling. The occurrence of induration and local parenthesis at the injection site is very rare [5]. Nervous system side effect such as headaches and dizziness. Digestive system side effect such as nausea, vomiting, diarrhea, and abdominal pain. Skin and subcutaneous tissue side effect such as itching, skin rashes, and urticaria. Muscular, skeletal and connective tissue systems side effect such as myalgia

and arthralgia. Symptoms of infections include fever and upper respiratory tract infections (rare). Fainting can occur up to 30 minutes after any vaccination but this study only induration that affected antibodies even though only contribute 14.8%.

Genetic with HPV Vaccination Antibodies

In this study genetic cancer in mothers, fathers, grandparents, grandparents totaling 19 children (43.8%) but that has formed adequate antibodies against cervical cancer 13 children (68.4%) cancer means there are still 31.6% who do not have adequate antibodies for neutralize the Human Papilloma virus. The results of this study indicate there is a genetic effect with antibodies after HPV vaccination, especially on the genetics of mothers, fathers and grandfathers proven p value <0.05. Respondents who have genetics have cancer as many as 5 people (11.4%). The types of cancer experienced by the respondent's family were 4 people (9.1%) and 2 people (4.5%) prostate cancer, whereas in this study there were no respondents who had a family history of cervical cancer. However, it is still necessary to administer HPV vaccinations to prevent or reduce the risk of cervical cancer. Family history such as mother and sister also determine the high potential for cervical cancer. At least the risk has doubled compared with those with no family history. This happens because in the family history there is the same immune system, cells carried by hereditary factors, as well as the immune system and the same infected factors (Center for Cancer Study info, 2014) [6]. Lubis (2017) research results explain that someone who has a family history of cervical cancer will be 3.3 times more likely to suffer from cervical cancer compared to those who have no family history [7].

Conclusion

- Positive antibodies after one-year HPV vaccination in elementary school children by 20%.
- Factors associated with positive and negative antibodies are mother, father, grandfather suffering from cancer, the presence of fever, itching, pain and unduration.
- Unduration is an important marker of the formation of antibodies after HPV vaccination.

Suggestions

- A booster (more HPV vaccination is needed)
- Evaluate antibodies after being given a booster.

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