

Correlation between HPV Vaccination and Cervical Cancer Incidence in Southeast Asian Population

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ABSTRACT

Human Papillomavirus (HPV) is the most common sexually transmitted disease of genital tract that may cause cervical cancer, the second most frequent type of cancer in South East Asia. By far, HPV vaccination is widely used for risk reduction; however, the rate of developing cervical cancer post-vaccination is still not well-studied. The aim of this study is to evaluate the association between HPV vaccination and development of cervical cancer in Southeast Asia. Analysis of data on HPV vaccination in Southeast Asia was performed, based on literature from 2010 to 2016 accessible in PubMed, Google Scholar, and ScienceDirect. Vaccination coverage rates and changes in cervical cancer incidence in particular countries were subjected to comparative analysis using Pearson's correlation coefficient. The statistical analysis showed HPV vaccination coverage and cervical cancer incidence has negative correlation but not significant ($r=-0.04$, $p>0.05$). This might due to HPV vaccination introduction is still at early stage (<10 years of implementation). In addition, 5 out of 9 countries are running the vaccination program as pilot project rather than nationwide program. Other factors may also influence the incidence of cervical cancer such as: genetics and lifestyle factor, socioeconomic status as well as having many children. Nevertheless, follow up study is needed to assess effect of HPV vaccination introduction and coverage to cervical cancer incidences in Southeast Asian countries.

Key words: Cervical Cancer, HPV, Southeast Asia, Vaccine

Human Papillomavirus (HPV) is the most common sexually transmitted disease of genital tract that has high risk cause cervical cancer.(1) Most of HPV infected do not have any symptoms/asymptomatic. However, the persistence of HPV infection may result in the development of cervical cancer.(2)

Current estimates of cervical cancer in the world in 2012 indicate 527.624 diagnosed annually and 265.672 are died from this disease. That makes cervical cancer as the fourth ranks cause of cancer death in the world.(3) While in Southeast Asia, cervical cancer become the second most frequent type of cancer, and become one of the highest incidence rates of cervical cancer in the world with 50.566 incidences and 23.989 number of deaths annually in 2012.(1)(4) In fact, data from World Health Organization (WHO) said that cervical cancer in Southeast Asia is

contributing to nearly 35% of the global burden of disease which become major public health program.(5)

Human Papillomavirus (HPV) associated with cervical cancer is considered as carcinogenic to human that based on the strong, consistent, and persistent between infections with the diseases.(6)(7) HPV vaccination is proved significantly reduces the HPV related disease; cervical cancer and provide high protection against it.(5)(2)

HPV vaccine works by stimulating antibody-mediated immunity, that will make neutralizing antibody before HPV virus infects the host cells by recognizing and inactivating it.(8) The vaccines that are available in the market: Cervarix, Gardasil, and Gardasil 9. Cervarix, only works for HPV types 16 and 18. Gardasil vaccine have the ability to high level of protection from types

6, 11, 16, and 18. While Gardasil 9 gives additionally protection against HPV types 6, 11, 31, 33, 45, 52, and 58.(1)(8) Both types of vaccines are approved in around 100 countries globally and have a known duration of protection of at least 5 years. However, since Gardasil 9 is still newer vaccine, it still has not been acceptable by WHO and approved in Asian countries yet.(1)

WHO recommended HPV vaccine should be implemented as national immunization programs and strategy by government in order to prevent cervical cancer. The strategy itself including training the health workers, give education, sexual, and reproductive health information to the people specially females about diagnosis, screening, and treatment of HPV related with cervical cancer, introduction to HPV vaccination as cervical cancer prevention. Especially, increased access to screening and treatment services.(9)(2)

Besides cervical cancer, HPV vaccine is found out to be effective in prevent other cancers from anogenital tract such as anus, vagina, penis, vulva, and oropharynx.(10)(8)

Therefore, HPV vaccination is offer simple and effective strategy widely to reduce the

risk of cervical cancer. However, the rate of developing cervical cancer post-vaccination is still not well-studied. The objective of this review is to evaluate the association between HPV vaccination and development of cervical cancer in Southeast Asia.

METHODS

Data Collection

Analysis of data on HPV vaccination in Southeast Asia was performed, based on literature from 2010 to 2016 accessible in PubMed, Google Scholar, and ScienceDirect, using the following keywords: "HPV vaccination", "Cervical Cancer", and "Southeast Asia".

For each included study, the following key information was extracted: country, vaccine coverage, vaccine status, year of introduction, and incidence of HPV (see appendix A1).

Statistical analysis

Vaccination coverage rates and change in cervical cancer incidence in particular countries were subjected to comparative analysis using Pearson's correlation coefficient with R software.

Table A1. Results of data collection

Country	Vaccine_Coverage	Vaccine_Status	Vac_Year	B_Inc	A_Inc	delta_inc
Brunei			2012-			
Darussalam	93	Y	2015	20	16.9	-3.1
Malaysia	94.33	Y	2010	16	15.6	-0.4
Vietnam	96	Pilot	Pilot	20.5	10.6	-9.9
Cambodia	77.8	Pilot	2015	38	23.8	-14.2
Indonesia	76.6	Pilot	2012	16	17.3	1.3
Lao PDR	76.9	Pilot	Pilot	17	12.5	-4.5
Philippines	70	Y	2015	21	16	-5
Singapore	8.8	Y	2010	13	8.1	-4.9
Thailand	60	Pilot	2014	19.5	17.8	-1.7

Vaccine_Status: Y = National Program; Vac_Year : Year of vaccine introduced; B_Inc : Incidence rate before Vaccine introduced; A_Inc: After vaccine intro; delt_inc : differences

RESULTS AND DISCUSSION

In this study, HPV vaccination coverage and incidence of cervical cancer of 9 Southeast Asia countries were collected (Brunei, Cambodia, Indonesia, Lao PDR, Malaysia, Philippines, Singapore, Thailand, and Vietnam). There are only nine out of eleven countries in Southeast Asia were subjected. Since there are no available data for Myanmar and Timor Leste and the HPV

vaccine in those two countries have not being introduced yet even become their national program.(4)

Five countries in Southeast Asia still in pilot program for HPV vaccine; Cambodia, Indonesia, Lao PDR, Thailand, Vietnam. Those countries that are still in pilot program may influence the data quality and may affect to the result. While the other four countries; Brunei, Malaysia, Philippines, and

Singapore already have their national program. In 2010, Malaysia and Singapore are being first countries that introduced HPV vaccination programs in ASEAN.(1)(11)

In the end, the result from statistical analysis showed HPV vaccination coverage and cervical cancer incidence in Southeast Asian population has negative correlation but not significant ($r=-0.04$, $p>0.05$). It might be due to limited data since there are two countries that are being eliminated; no data available from Myanmar and Timor Leste, five out of nine countries (Cambodia, Indonesia, Lao PDR, Thailand, Vietnam) are running the vaccination program as pilot project rather than nationwide program, while only four countries (Brunei, Malaysia, Philippines, and Singapore) have their

nationwide program for HPV vaccination, Malaysia and Singapore the first countries that introduced it in Southeast Asia.

In addition, several factors may also influences the result; first the HPV vaccine in developing country, the database system that record medical activity is not well established and other factors like genetics and lifestyle factor, socioeconomic status as well as having many children. Such factors might produce less statistically powerful result. Moreover, to achieve more powerful result, establishment of a system to record medical activity is required. In order to analyze in more reliable and valid data to evaluate association between HPV vaccination and cervical cancer more deeply

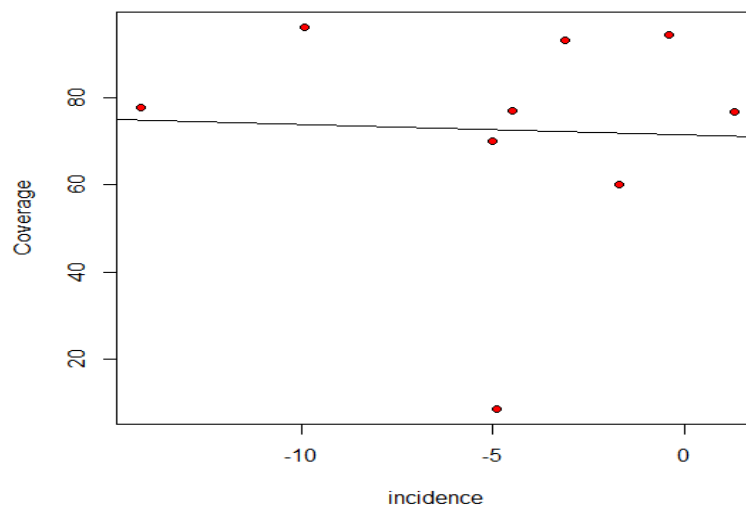


Figure A2. Scatter plot of HPV vaccination against cervical cancer

CONCLUSION

Overall, the analysis showed it is not really significant result. Since HPV vaccination introduction is still at early stage (<10 years of implementation). Nevertheless, follow up study is needed to assess effect of HPV vaccination introduction and coverage to cervical cancer incidences in Southeast Asian countries

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REFERENCES

1. **Amfar.** Cervical Cancer, Human Papillomavirus (HPV), and HPV Vaccines in Southeast Asia. 2016;(November).
2. **WHO.** Human Papillomavirus Vaccines: WHO Position Paper. Vol. 19, Weekly Epidemiological Record. 2017. p. 241–268.
3. **Bruni L, Barrionuevo-Rosas L, Albero G, Serrano B, Mena M, Al E.** Human Papillomavirus And Related Diseases In The World. ICO Information Centre On HPV And Cancer (HPV Information Centre); 2017.

4. **Bruni L, L B-R, Albero G, Serrano B, Mena M, Gómez D, et al.** Human Papillomavirus And Related Diseases In Myanmar. ICO Information Centre On HPV And Cancer (HPV Information Centre); 2017.
5. **Domercant J, Guillaume F, Marston B, Lowrance D.** Strategic framework for the comprehensive control of cancer cervix in South-East Asia Region. Vol. 64, MMWR. Morbidity and Mortality Weekly Report. 2015. 137-140 p.
6. **Basu P, Banerjee D, Singh P, Bhattacharya C, Biswas J.** Efficacy and Safety of Human Papillomavirus Vaccine for Primary Prevention of Cervical Cancer: A Review of Evidence From Phase III Trials and National Programs. *South Asian J Cancer*. 2013;2(4):187=192.
7. **Norman I.** Human Papillomavirus and Cervical Cancer: Detection of Potential Markers of Disease Progression Using Liquid-Based Cytology (Doctoral Dissertation, Karolinska Institutet, Stockholm, Sweden). 2015; Available from: <http://hdl.handle.net/10616/44555>
8. **Takes R., Wierzbicka M, D'Souza G, Jackowska J, Silver C., Al E.** HPV Vaccination To Prevent Oropharyngeal Carcinoma: What Can Be Learned From Anogenital Vaccination Programs? *Oral Oncol* [Internet]. 2015; Available from: <http://dx.doi.org/10.1016/J.Oraloncology.2015.10.011>
9. **Setiawan D, Oktora M., Hutubessy R, Riewpaiboon A, Postma M.** The Health-Economic Studies Of HPV Vaccination In Southeast Asian Countries: A Systematic Review. *Expert Review Of Vaccines*. 2017;
10. **De Vuyst H, Clifford G., Nascimento M., Madeleine M., Franceschi S.** Prevalence and Type Distribution of Human Papillomavirus in Carcinoma and Intraepithelial Neoplasia of The Vulva, Vagina And Anus: A Meta-Analysis. *Int J Cancer*. 2009;124:1626–1636.
11. **Bruni L, Diaz M, Barrionuevo-Rosas L, Herrero R, Bray F, Al E.** Global Estimates of Human Papillomavirus Vaccination Coverage by Region and Income Level: A Pooled Analysis. *Lancet Glob Heal*. 2016;4:E453–63.