Adverse Event Following HPV Vaccination in Thailand 2017 – July 2024

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INTRODUCTION

HPV is a common sexually transmitted infection linked to cervical cancer in women and oropharyngeal cancer in men. HPV types 16 and 18 are responsible for 70% of cervical cancer cases globally. Vaccination and screening greatly reduce cervical cancer rates, though healthcare disparities remain an issue. In 2022, the WHO recommends vaccinating girls aged 9-14. **Thailand initiated a school-based HPV vaccination program in 2014 for fifth-grade girls**, but vaccine shortages disrupted the program between 2019 and 2022. **In 2023, a renewed campaign targeting females aged 11-20 aimed to administer at least 1 million doses by year-end**. This study describes the characteristics of adverse events (AEs) following HPV vaccination before and after the comprehensive 2023 campaign.

METHOD

Study Design: Descriptive studywas conducted by reviewing the adverse events (AEs) following HPV vaccination in Thailand reported to the national AEFI surveillance system (AEFI-DDC) in Thailand between 2017 – July 2024.

HPV vaccine administration data were extracted from Health Data Center, Ministry of Public Health.

Study definition:

- **AEFI:** Any untoward medical occurrence within 30 days of vaccination,regardless of causal relationship.
- **Serious AEFI:** Severe AEs resulting in hospitalization for more than 24 hour or prolongation of a pre-existing hospitalization; significant dysfunction and/or persistent disability; congenital anomaly; risk of death or death
- **AEFI cluster**: Two or more cases occurring in a similar or related manner in terms of timing, vaccination location, and/or vaccine type.

Descriptive statistics were employed to summarize the data. Continuous variables, such as age, were expressed as mean, median and range, while categorical variables, such as gender, were presented as frequencies and percentages. Results were divided into two periods pre- and post-2023 campaign phases.

RESULT

- Between **2017 and July 31st , 2024**, **165 adverse event reports** following HPV vaccination were recorded in the AEFI surveillance database. **During this period, 2,756,628 HPV doses were administered in Thailand**, with an **overall reporting rate of 5.98 per 100,000 doses**. **All the reported AEFIs occurred in young women**; the **median age 11 years** (10-21).
- Of the 165 cases, **11 (7%) were classified as serious**, with a rate of **0.4 per 100,000 doses**, while **159 (93%) were non-serious**, with a rate of **5.6 per 100,000 doses**.**Non-serious AEs** included dizziness, nausea, headache, rash, and vomiting.
- **Of the 11 serious AEs, 3 deaths were reported.** The serious cases included 3 with seizures, 2 with anaphylaxis, and 1 each with HHE, facial palsy, intracerebral hemorrhage, SJS-TEN, myocarditis, and unknown cause of death.
- **Among 3 fatal cases,** the National Expert Committee (NEC) on AEFI determined that one death was an indeterminate event, one coincidental, and one unclassifiable event.
- **The AE reporting rate was significantly higher during the initial program phase compared to 2023-2024** (8.02 vs. 4.32 per 100,000 doses, p < 0.01), though **serious AE rates did not differ significantly** between the periods (0.20 vs. 0.34 per 100,000 doses, p < 0.13).
- **11 clusters of AEs were reported** across seven provinces, with cluster sizes ranging from 3 to 24 cases. The largest cluster, coincided with the first nationwide HPV vaccination campaign targeting fifth-grade elementary school students.
- **The most common symptoms reported were dizziness, headache, nausea, and dyspnea (difficulty breathing).** All young women had a complete resolution of the clinical manifestation, without any specific treatment or sequelae. The medical investigation concluded that the events were likely "**immunization stress related response (ISRR)**".

Table 1 Number of AEs following HPV vaccination, and reporting rates (per 100,000 doses administered), in Thailand, 2017 to July 31st, 2024

Year	Number of HPV vaccine doses administered	All AEFI report		Serious AEFI report	
		Number of cases	Rate per 100,000 HPV doses	Number of cases	Rate per 100,000 HPV doses
2017	290,962	41	14.1	0	0
2018	587,911	37	6.3	2	0.3
2019	117,878	2	1.7	0	0
2020	No data due to vaccine shortage	9	NA	3	NA
2021		0	0	0	0
2022		0	0	0	0
2023	1,127,168	70	6.2	3	0.3
2024*	632,709	6	0.9	3	0.5
Total	**2,756,628**	**165**	**5.9**	**11**	**0.4**

* Data as of July 31st, 2024
$ NA; a reporting rate per 100,000 doses administered could not be calculated due to a lack of HPV vaccination data.

Table 2 Characteristic of report of AEs following HPV vaccination, Thailand, from 2017 to July 31st, 2024

Characteristic	Total	Before the comprehensive 2023 campaign*	After the comprehensive 2023 campaign	p-value
HPV Vaccine administered	2,756,628	996,751	1,759,877	-
Number of AE report (cases, reporting rate per 100,000 doses administered)	156 (5.66)	80 (8.02)	76 (4.32)	< 0.01
Seriousness (cases, reporting rate per 100,000 doses administered)				
- **Non-serious AE**	148 (5.37)	78 (7.82)	70 (3.98)	< 0.01
- **Serious AE**	8 (0.29)	2 (0.20)	6 (0.34)	< 0.13

* The adverse event reporting data for 2020 was not included in the calculation due to the lack of HPV vaccination data for that year.

CONCLUSION AND RECOMMENDATION

The HPV vaccine in Thailand has a generally favorable safety profile,with lower AE reporting rates compared to some other countries.While serious adverse events are rare, continuous monitoring is crucial. Moreover, preparedness for cluster of immunization stress-related reactions (ISRR) during mass campaigns are necessary. Further studies with larger samples and ongoing surveillance are important to ensure vaccine safety and detect any rare or delayed effects.

LIMITATION

- Some reported data may be incomplete or inaccurate due to initial diagnoses provided by treating physicians may not have been confirmed by laboratory
- **The transition to an online reporting platform during the study period** may have affected data completeness.
- The study may have been affected by **underreporting of AEs and vaccine doses administered in the private sector.**

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