



PPUKM PHARMACY BULLETIN

VOLUME 1, ISSUE 3

2015

Updates on Human Papillomavirus (HPV) Vaccine Safety by PRP Kam Siew & Izyan

In January 2015 this year there were circulating rumours that went viral regarding severe and life threatening adverse reaction of human papilloma virus (HPV) vaccine which occurred in Columbia, Australia and Europe. The highlight of the messages were how school children had major adverse reaction including death days after receiving the HPV vaccine. Subsequently the 'anonymous' message urged parents not to give their consent for HPV vaccination offered by the Ministry of Health (MOH) Malaysia which has been part of the National Immunization Program (NIP) since 2010. The unscrupulous news stated that HPV immunization was unsafe and hundreds of teenagers suffered from symptoms of anemia, fatigue (malaise) and fainting (loss of consciousness) hours/days after getting the vaccination.

The rumors raised concerns among worried parents with schooling children; and this issue was quickly addressed by Dr Chong Chee Keong, Director of Disease Control, Ministry of Health Malaysia. In his recent official statement on 23rd January 2015, Dr Chong said the Ministry of Health had reviewed the details of the Columbia-HPV vaccine incident with World Health Organization (WHO). It was found out that of the 240 cases occurred, only 11 cases were confirmed by Colombian Ministry of Health. Colombia's Health Ministry stated that there was no strong evidence linking these symptoms with the HPV vaccine. Furthermore an independent body conducting investigations into the incident concluded that the symptoms experienced were *mass psychogenic response* to immunization. Below are the reported incidence about HPV vaccine.



Claimed Incidences

- Cctv-america.com reported that more than 240 girls in El Carmen de Bolivar, Columbia have been hospitalized after receiving shots of Gardasil® due to headache, fainting and numbness in the hands. However, only 11 cases were confirmed by Colombia.
- 26 teenagers in Australia suffered spells of dizziness, blackouts and neurological symptoms after HPV vaccination but only 4 cases were admitted and all of them recovered without complications.
- Two reports on sudden and unexpected deaths of two young women in the European Union (EU) ^[1]; one occurred in Austria and the other in Germany. In both cases, the cause of death could not be identified. No causal relationship has been established between the deaths of the young women and the administration of Gardasil.

Findings & Conclusion from Health Authorities



- In the **United States (US)**, Vaccine Adverse Event Reporting System(VAERS) have received a total of **96** reports of death after receiving the Gardasil vaccine between June 2006 and March 2014. Although there were reported death cases to VAERS but that **does not conclude** that the **vaccine caused the death**. Out of the 96 death reports received, only 47 could be verified while the rest unverified as there was lack of information reported. Detailed review of every report of death shows that there is **no causal relationship** that suggests Gardasil vaccine caused the deaths. Moreover there is no trend of death with respect to time after vaccination.
- *The Vaccines and Related Biological Products Advisory Committee (VRBPAC)* reported that, serious adverse events (SAEs) or deaths between Gardasil groups and placebo groups in the clinical trials were similar in frequencies. They concluded that those adverse events and the deaths (caused either by traumatic injuries or drug overdose, etc.) were not related to vaccine under the study^[6]. Similar findings were noted for European Medicines Agency (EMA). EMA's Committee for Medicinal Products for Human Use (CHMP) supports that the **benefits** of Gardasil **outweigh its risks**. Nevertheless continuation monitoring of safety shall be done^[2]
- Ministry of Health Malaysia will take preventive measures in view of the recent incidence in Columbia. To prevent these symptoms the vaccine is administered with the students seated and placed under supervision for 15 minutes after the immunisation.

National Immunization Programme [NIP] in Malaysia

In Malaysia, free school based vaccination is given to all Form 1/Year 7 students irrespective of actual age registered in public, private and international schools starting 2010. This is a voluntary HPV vaccination with parental consent. For those out of school 13 years old girl, clinic based vaccination are available^[5].



Human Papilloma Virus Vaccine Facts : What We Already Know

Vaccine is a biologically prepared agent that is made from weakened or killed forms of the microbe, its toxins or one of its surface protein^[4]. HPV vaccine helps prevent HPV infection and precancerous conditions that may lead to cervical cancer if it is given prior exposure to the HPV types contained in the vaccine. In Malaysia, there are 2 HPV vaccines available; the bivalent Cervarix® and the quadrivalent Gardasil®. Gardasil® contains two types of high risk genotypes HPV (type 16 & 18) and two types of low risk genotypes (Type 6 & 11). Gardasil® protects against genital warts and anal cancer in both males and females, in addition to prevent cervical cancer, vulvar cancer and vaginal cancer among females.

HPV is a DNA virus that infects epithelial (skin or mucosal) cells at the genital area and can cause cervical cancer in women^[3]. It can be transmitted by normal sexual intercourse, oral sex, anal sex or any other contact involving the genital area. There are more than 40 types of HPV, only 4 are of greater concern; HPV 6, 11, 16 and 18 respectively^[4]. Type 6 & 11 can cause genital warts while HPV 16 and 18 can cause cervical cancer. It's not very common, but sometimes a pregnant woman with HPV can pass it to her baby during delivery. In these cases, the child can develop recurrent respiratory papillomatosis (RRP), a rare condition where warts caused by HPV (similar to genital warts) grow in the throat.

On 14th December 2014, FDA approved **Gardasil 9®** to prevent cervical, vulvar, vaginal and anal cancers. Gardasil 9 has five additional HPV types—31, 33, 45, 52 and 58— which cause approximately 20 percent of cervical cancers and are not covered by previously FDA-approved HPV vaccines.

FACTS of Cervical Cancer in Malaysia

- Cervical cancer is the **third** most common cancer (8.4%) among females in Malaysia and fifth most common cancer in the entire general population. The most common type of cancer among females is breast cancer (32.1%) followed by colorectal cancer (10%)⁷.
- Fourth commonest cause of death in women in Malaysia.⁹
- Around 8.7 million women over the age of 15 in Malaysia are at risk⁹ and about 6 women are diagnosed with cervical cancer every day⁹.
- Many present at an advanced stage of the disease when the outcome is poor and half of them die from the disease⁹.
- Almost all cases of cervical cancer are caused by HPV.
- Cervical cancer incidence rate increase after 30 years old and peaks at ages 65-69 years. Compared among the major races, Indian women had the highest incidence for cervical cancer followed by Chinese and Malay⁷.
- The annual cervical cancer death rate is 5.6 per 100,000 (Cervical Cancer Incidence and Mortality Rates 2011). The mortality rate due to cervical cancer in Malaysia is more than two times higher than the Netherlands, United Kingdom and Finland⁸.
- It costs about RM312 million (USD76 million) to manage cervical cancer (from prevention to managing invasive diseases) annually in Malaysia. A big proportion (67%) of this is spent to manage invasive cancer⁸.
- Cervical screening services available nationwide but the uptake rates were only 26% in 1996 and 43.7% in 2006
- **RM3.45 million doses** of HPV vaccines have been used with 60% being quadrivalent HPV vaccines.
- Gardasil® prevents at least **6 types of cancer** (cervical, anal, vulva, vaginal, oropharyngeal and penile). To date, these are the only preventable cancers that can be preventable.

Worldwide Health Authorities Recommendations on SAFETY & EFFICACY of HPV Vaccine

- HPV vaccine is the result of more than 10 years of research and development.
- Its efficacy was established in clinical trials involving more than 25,000 females and males.
- Several real-world outcome studies have supported the efficacy data from the clinical trials.
- Outcome studies in several countries showed a significant reduction in the prevalence of HPV infection and cervical lesions which preceded cancer, following HPV vaccination, thus protecting girls from cervical cancer.
- HPV vaccines have an excellent safety profile.
- Safety has continued to be evaluated in several large post-licensure surveillance studies in more than 500,000 people following administration.
- In March 2014, the WHO's Global Advisory Committee on Vaccine Safety (GACVS) stated that they have not found any safety issue that would alter any of the current recommendations for the use of HPV vaccines, and reaffirmed the favorable benefit-risk profile of HPV vaccines.
- GACVS reiterated "allegations of harm from vaccination based on weak evidence can lead to real harm when, as a result, safe and effective vaccines cease to be used."
- While no vaccine or medicine is completely without risk, leading international health organizations such as the World Health Organization (WHO), the US Centers for Disease Control and Prevention (CDC), Health Canada, the European Medicines Agency (EMA), the Australia Therapeutic Goods Administration (TGA), have continued to recommend the use of HPV vaccines.
- According to Jabatan Kemajuan Islam Malaysia; JAKIM, 2012:123-125 following the *Muzakarah Jawatankuasa Fatwa Majlis Kebangsaan Bagi Hal Ehwal Ugama Islam Malaysia on Hukum Pengambilan Vaksin Human Papilloma Virus (HPV)*:
"Muzakarah bersetuju memutuskan bahawa pengambilan Vaksin Human Papilloma Virus (HPV) yang telah dipastikan tiada unsur meragukan dalam kandungannya dan tidak mendatangkan kemudharatan adalah diharuskan bagi mencegah penyakit kanser pangkal rahim (servik) di kalangan wanita."

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A publication of : DRUG INFORMATION CENTRE

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