

## RESEARCH COMMUNICATION

# Human Papilloma Virus Vaccination in Nepal: An Initial Experience

Yogendra Singh\*, Aarti Shah, Meeta Singh, Sheela Verma, Bhakta Man Shrestha, Prabhu Vaidya, Radha Pyari Nakarmi, Surendra BB Shrestha

### Abstract

Cervical cancer is the commonest cancer among women in Nepal. Human papilloma virus (HPV) infection, a recognized cause of cervical cancer, is very common in sexually active women and HPV vaccination has been recommended as a prophylactic therapy. If HPV infection is prevented by the HPV vaccination to the adolescent girls, cervical cancer is also prevented. We received 3,300 vials of quadrivalent human papilloma virus (types 6, 11, 16, 18) recombinant vaccine (Gardasil; Merk & Co.) as a gift from the Australian Cervical Cancer Foundation (ACCF) which has a mission to provide life-saving HPV cervical cancer vaccines for women in developing countries, who cannot otherwise afford vaccination. HPV vaccine was offered to 1,096 of 10 to 26 year aged girls attending 17 secondary schools. In total, 1,091 (99.5%) received the second dose and 1,089 (99.3%) received the third dose of the vaccine. The remaining 5 girls at second dose and 2 girls at third dose remained unvaccinated. No serious vaccine related adverse events were reported except mild pain at the injection site in 7.8% of the vaccine recipients. High cost and low public awareness are the key barriers for successful implementation of the vaccination program in resource limited developing countries. In conclusion, HPV vaccine is safe with high acceptability in Nepalese school girls. However a large population study for longer follow up is warranted to validate the findings of this vaccination program.

**Keywords:** Acceptability - cervical cancer - feasibility - HPV vaccine - side effects

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### Introduction

Cervical cancer is the second most common cancer & a leading cause of cancer mortality among women worldwide. The majority of the cervical cancer mortality occurs in the developing countries where screening & optimal treatment are not adequately available (WHO, 2007). A recent multi-institution hospital-based cancer incidence data reveal cervical cancer as the most common cancer among women in Nepal (Pradhananga et al., 2009). Genital Human Papilloma Virus (HPV) infection is the most common sexually transmitted infection among sexually active couples (Woodman et al., 2001; Woodman et al., 2007). Around 3/4<sup>th</sup> of sexually active men and women have been exposed to HPV at some point in their lives. Cervical cancer has been recognized as an outcome of HPV-16 and -18 infections in around 70% (cancer.gov, 2007). If HPV infection is prevented, cancer will not occur. Zur Hausen H, Winner of the Nobel Prize in Physiology or Medicine in 2008 for his discovery of the oncogenic HPV causes cervical cancer, led the foundation of prophylactic vaccines against HPV infection (Zur Hausen, 2002). Evaluation of the HPV vaccine efficiency in preventing cervical dysplasia and cancer has been recommended as a globally accepted endpoint for population based studies

(Ljubojević, 2006). The HPV vaccine that has been approved by the US Food and Drug Administration (FDA) is the quadrivalent vaccine that consists of recombinant viral-like particles (VLPs) of HPV 6, 11, 16, 18 mixed with an aluminum-containing adjuvant. In March 2008, we received 3,300 vials of quadrivalent human papilloma virus (types 6, 11, 16, 18) recombinant vaccine (Gardasil; Merk & Co.) by Australian Cervical Cancer Foundation (ACCF). ACCF's vision is to protect and enhance women's health by eliminating cervical cancer and enabling treatment for women with cervical cancer and related health issues, in Australia and in developing countries. One of the ACCF's aims is to provide life-saving HPV cervical cancer vaccine for women, in developing countries, who cannot otherwise afford vaccination. The objective of this study was to assess the feasibility, acceptability and adverse events of a delivering a HPV vaccine to adolescent schoolgirls in Nepal.

### Materials and Methods

HPV vaccine, the quadrivalent Human Papillomavirus Virus-Like Particle Vaccine (Gardasil), is a sterile liquid suspension prepared from the highly purified virus-like particles of the recombinant major capsid (L1) protein of

HPV Types 6, 11, 16 and 18. Each 0.5 ml dose contains approximately 20 mcg of HPV6 L1 protein, 40 mcg of HPV11 L1 protein, 40 mcg of HPV16 L1 protein and 20 mcg of HPV18 L1 protein. Each dose of the vaccine contains approximately 225 mcg of aluminum (as amorphous aluminum hydroxyphosphate sulphate adjuvant), 9.56mg of sodium chloride, 0.78mg of L-histidine, 50 mcg of polysorbate, 80.35 mcg of sodium borate and water for injection.

Gardasil is a sterile cloudy white liquid, which is stored refrigerated at 2 to 8°C and protected from light. It was administered as soon as possible after being removed from refrigeration. The vaccine was administered intramuscularly in the deltoid region of the upper arm or in the higher anterolateral area of the thigh. For the single use vials a separate sterile syringe and needle was used for each individual. The vaccine was used as supplied, no dilution or reconstitution was necessary. Each single use vial of Gardasil costs more than 100 USD. In March 2008, the Nepal Australian Cervical Cancer Foundation (NACCF) and at that time working through Nepal Network for Cancer Research and Treatment, Banepa, Nepal received 3300 vials of HPV vaccine as a gift by the sister organization, ACCF.

In April 2008, 1096 school girls aged 10 to 26 years from 17 secondary schools from Kavre District and Kathmandu Valley were selected for HPV vaccination. Each school developed a plan to implement delivery of the vaccine at 0, 2 and 6 months and a process for reporting any side effects. Parents, teachers and girls were fully informed about the vaccination program. Written consents were obtained.

## Results

HPV vaccine was offered to 1096 of 10 to 26 years aged girls attending 17 secondary schools. All pre-vaccination registered school girls received the first dose of the vaccine. The majority of the girls (90%) were in the age group 12 to 16 years (Table 1). In total, 1091 (99.5%) received the second dose and 1089 (99.3%) received the third dose of the vaccine (Table 2). The remaining 5 (0.5%) girls at second dose and 2 (0.7%) girls at third dose remained unvaccinated. Mild pain at the injection site was observed in 75 girls (7.8%). No serious vaccine related adverse events have been reported so far.

## Discussion

Cervical cancer is the major cause of cancer morbidity and mortality worldwide but it is a burning issue in developing countries including Nepal. Screening and HPV vaccination are the key steps for cervical cancer prevention. In our part of the world, some efforts are made to implement the reliable method of cervical cancer screening (Sankararayana et al., 2008). Treatment of the precancerous lesions will certainly prevent cervical cancer. On the other hand, HPV vaccine targeted against two types of oncogenic HPV can eliminate approximately 70% of all invasive cervical cancers. Therefore, vaccination against HPV infection will ultimately decrease the incidence of

**Table 1. Age of the Schoolgirls Vaccinated with HPV Vaccine (Gardasil)**

Age (Year)	No.	%
10	4	0.4
11	4	0.4
12	115	10.5
13	196	17.9
14	269	24.5
15	261	23.8
16	145	13.2
17	67	6.1
18	24	2.2
19	5	0.5
20	3	0.3
21	1	0.1
26	2	0.2
<b>Total</b>	<b>1096</b>	<b>100</b>

**Table 2. HPV Vaccine (Gardasil) Vaccination Data**

Vaccination Schedule	Age of the girls	No. of the girls	Drop out girls
1 <sup>st</sup> Dose	10-26 year	1096	0
2 <sup>nd</sup> Dose	10-26 year	1091	5
3 <sup>rd</sup> Dose	10-26 year	1089	5+2
Total		3276*	12** (0.36%)

\* NNCTR/INCTR Nepal received 3300 vials of Gardasil Vaccine from ACCF in 2008. Out of 3300 vials, 12 vials were donated to Bhutan and \*\*12 vials were unused.

cervical cancer in near future (Mandic and Vujkov, 2007). Various multicentric clinical trials have demonstrated very high efficacy of the HPV vaccine in preventing precancerous cervical, vulval and vaginal lesions (Merk. Com, 2006). The vaccine must be given prior to infection that is prior to the onset of sexual activity.

The problems of successful implementation of the HPV vaccination in developing countries like Nepal may include the affordability, delivery of the vaccine nationwide and public unawareness about the disease (Prasai, 2008). Most of the people cannot afford this vaccination. The cold chain maintenance is another challenge due to lack of the electricity or irregular electric power supply. The most important factor is lack of awareness about HPV infection and cervical cancer. The knowledge of HPV vaccination is also lacking among physicians (GSK, 2007). We need to increase our education and communication efforts for awareness among medicos as well as public in general. Continuous targeted educational and awareness programs are organized for healthcare professionals, media, patients and parents in order to increase vaccine acceptance (Herzog et al., 2008). In this vaccination program, HPV vaccination acceptance was high despite low levels of knowledge of HPV. The number of HPV vaccines available was limited. One of the reasons for high acceptability may be related with affordability of the vaccine in Nepal. On other hand, women are more accepting a cervical cancer vaccine if they are associated with negative consequences with the

disease (Fazekas et al., 2008).

As HPV vaccines are not live vaccines, there should not be any vaccine safety problem. These vaccines are based on the virus particle technology consist of outer coat viral protein (L1) and no viral RNA or DNA required for viral replication or oncogenesis. The adjuvant in the HPV vaccines is aluminum base which is widely used in other vaccines (Ulanova et al., 2001).

The majority of adverse events of the HPV vaccination are minor, whilst the incidence of serious adverse events is balanced between vaccine and control groups (Rambout et al., 2007). Local reactions at the injection site (pain, redness and swelling) are significantly more frequent in vaccine than placebo recipients. However, serious vaccine related adverse events are rare (<0.1%) (Agorastos et al., 2009). This recent review concludes that HPV vaccines are safe and effective vaccines for women's health.

In conclusion, HPV vaccine is safe with high acceptability to adolescent schoolgirls. High cost and low public awareness are the key barriers for successful implementation of the vaccination program in resource limited countries like Nepal. A long term large study is warranted to see the outcome of the prophylactic vaccination against HPV infection in Nepal.

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