



Cervical Cancer

Cervical Cancer HPV Vaccination and Bhutan

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South Asian J Cancer 2023;12(1):41–43.

Introduction

Bhutan is a small landlocked kingdom whose name means the land of the thunder dragon. It is a carbon-negative country that has pledged to have more than half of the country dedicated to forests. Television and internet were allowed in the country as late as 1999. King Jigme Singye Wangchuck gave up monarchy and handed over to democracy in 2005.

Right to health is very important here. This is the only country in the world that emphasizes Gross National Happiness. This unique Bhutanese concept has a deep implication and has several dimensions. It is truly holistic—based on people's spiritual, material, social, and physical needs. It envisions a pragmatic progress, dependent on ecologic sustainability for current and future generations, as well as a balanced distribution of well-being among its entire people.¹ To this objective, they have also banned the sale of tobacco.

In Bhutan, about a 10th (7.4–11.4%) of government spending is on health. No wonder Bhutan has achieved 91.8% of health metrics based on country's income.² Yet catastrophic health expenditure occurs in 0.51%, impoverishment in 0.32% cumulative financial hardship is seen in 2.55% of the population.³

Cancers remain a challenge. Cervical cancer is the third most common cancer (and number 1 among women) and is the fifth largest cause of mortality.^{4,5} With the median age of

the population being 22.3 years and almost 33% contributed by those younger than 14 years, tackling this disease is vital.

With a female population of 3.58 lakhs in 2019, the age-standardized incidence of cervical cancer was 14.2 per 1 lakh. Impressively, 40% of eligible females are covered by cervical cancer screening programs (2015–2019). The mortality to incidence ratio remains 0.57.⁶

One cross-sectional study of women (average age 23 years) who attended national graduate orientation program revealed low cervical cancer knowledge as well as poor screening behavior.⁷ A total of 94% had never undergone a cervical cancer screening. Reasons cited included not knowing its necessity, unwillingness to be examined by a male health worker, and dread of being diagnosed with cancer.

In another important study, paired samples of urine and those of exfoliated cervical cells from 89 women with history of high-risk human papillomavirus (HPV) positive and normal cytology were studied.⁸ The sensitivity of urine to detect 21 HPV types (with cells as gold standard) was 80% for E7-MPG and 58% for GP5 +/6 +. The specificity was 61 and 89%, respectively. Interestingly, the HPV type distribution in urine and cells was similar, regardless of assay. This showed that it is possible to use urine testing to detect HPV.

Vaccination has been a strong point of Bhutan. Let us take the example of its vaccination against coronavirus disease 2019 implementation (started on March 27,

DOI <https://doi.org/10.1055/s-0043-1764220> ISSN 2278-330X

How to cite this article: Hingmire S, Tshomo U, Dendrup T, et al. Cervical Cancer HPV Vaccination and Bhutan. South Asian J Cancer 2023;12(1):41–43.

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2021). Within an ultrashort period of 2 weeks, more than 90% of the eligible adult population (18 years and older) had received the first dose.⁹ This was possible thanks to the generosity of Government of India that provided 550,000 doses of Covishield. Interestingly, the conservative and highly religious Bhutan used astrology to start the national project at the auspicious time of 9.30 a.m., by vaccinating Ninda Dema, a 30-year-old woman born in the monkey year.

Hence, its national HPV vaccination program was also expected to be successful. It was initiated in 2010 and has been able to achieve more than 90% coverage. This flagship program to eliminate cervical cancer has now also started by vaccinating adolescent boys and girls since 2020.¹⁰ It is expected that major achievements, including reduction in incidence and mortality of cervical cancer, shall be achieved by the year 2030.

But Is This Realistic?

Cervical cancer directly due to HPV infections is highest (73%) among low- and middle-income countries (LMICs). Most of these are not in a position to implement HPV vaccination at the national level. A recent meta-analysis was able to identify gaps, issues, and challenges.¹¹ Up to 2021, less than 30% LMICs have included HPV vaccination as part of their national immunization schedule. For their meta-analysis, 135 countries were grouped as LMICs using World Bank criteria (gross national income per capita in 2019). Articles published in the English language in PubMed, Scopus, Web of Science, or CENTRAL databases up to October 2020 were evaluated for inclusion. Primary end point was measurement of number of eligible people who took at least one dose of HPV vaccine.

Forty-seven of 4,267 published studies evaluated were found to be eligible for meta-analysis and were included. These included 4,338,331 participants of which 4,336,836 (99.97%) were females. At least one dose of the HPV vaccine was administered in 3,325,779 individuals (76.7%). In Bhutan, the compliance to first dosing was an impressive 96.1%. Studies reported the use of diverse strategies and incentives to make the initial projects successful—including active communication strategy that included community leaders, teachers, and parents; token incentives such as t-shirts and bracelets; and financial contributions towards cost of participation as well as retention of the vaccinated cohort up to project completion. Compliance was associated with desire to protect their daughters from occurrence of cervical cancer and availability of the vaccine without cost. Noncompliance was attributable to parent/caregiver fear about the vaccine; inconvenient location/time for the vaccination; lack of understanding/knowledge; and forgetfulness. Vaccination was either supported by governments of respective countries (such as in Bhutan) or with the help of nongovernmental organizations.

Since HPV vaccination became available in 2006, those who were vaccinated are now in their 20s. In this age group (20–24 years), incidence of invasive cervical cancer has fallen by about 3% every year from 1998 to 2012. After

that (2012–2019), it fell by 11.4% every year. Thus, the reduction in rates of cervical cancer is 65% (2012–2019) as compared to a fall of 33% (2005–2012), an impressive doubling. In the United States, this reduction is seen across different ethnic groups (64% in Caucasians; 69% in blacks; and 70% in Hispanic).¹²

The meta-analysis showed that approximately 3.3 million females received the vaccination (between 2015 and 2020) as compared with 1.4 million earlier (between 2006 and 2014). Unfortunately, among the LMICs, full course of vaccination was possible in only 1% of the 47 million eligible women. In addition, once the demonstration projects were completed (withdrawal of earmarked funding), the uptake of HPV vaccination dropped significantly (for countries with 89.4% uptake up to 2014, the figure dropped to 41.48% post 2014). Thus, financial constraints remain the major bedbug in achieving the World Health Organization (WHO)'s objectives regarding HPV vaccination and cervical cancers.

For WHO's strategy for 2030 to be successful, about 10.5 billion USD would be needed—based on the cost of Gardasil, Cervarix, Gardasil-9, and Cocolin. Fortunately, the cost can be reduced substantially with the availability of the Cervavac (quadrivalent HPV vaccine) developed by Department of Biotechnology, Government of India and Serum Institute of India.¹³

Conclusion

Cervical cancer remains a major health care challenge in Bhutan. The national HPV vaccination program has been quite successful with a 90% coverage. However, logistics of the last mile continue to throw up new problems. In order for the WHO's strategy to be successful by the year 2030, HPV vaccination program will have to be strengthened. Fortunately, the availability of the quadrivalent Cervavac from India will substantially reduce cost and ease this most important challenge.

Conflict of Interest

None declared.

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