

Cervical Cancer and Ethical issues in HPV Vaccination

Fariha Haseen¹, Sadia Akther Sony²

1. Assistant Professor Department of Public Health and Informatics
Bangabandhu Sheikh Mujib Medical University. Email: farhaseen3@gmail.com

2. Research Program Manager
Department of Public Health and Informatics, Bangabandhu Sheikh Mujib Medical University

Abstract: Human Papilloma Virus (HPV) infection causes death of 270,000 people die from every year. Sexually transmitted HPV was found one of the major causes of cervical cancer. World Health Organization (WHO). Cervical cancer (CC) is one of the top five cancers that affect women around the world. In June 2006, the Food and Drug Administration (FDA) approved a new vaccine for women, Gardasil, produced by the pharmaceutical company Merck that protects against infection by certain strains of HPV, including the two strains that cause most cases of cervical cancer. Vaccinations are counted as one of public health's important development but there is an ethical dilemma between balancing personal autonomy and protection of the entire at risk population. The vaccine caused very few side effects like local reactions whereas signs or symptoms of greater importance were very. Moreover it was considered that the vaccine is has an efficacy of practically 100% in prevention of precancerous lesion caused by the viral genotypes included in the vaccine. Bioethicists were not convinced about compulsory vaccination laws as the values of patient autonomy and informed consent to be preeminent to them. Not surprisingly, some have expressed wariness about or opposition to mandating HPV vaccination. A critical question is whether achieving a higher level of coverage justifies the infringement on parental autonomy that compulsory vaccination inevitably entails. Recommendation of the universal vaccination of girls and young women may evolve ethical challenges which might make it difficult for smooth implementation of the vaccination campaigns. Review of the ethical issues in HPV vaccination will constitute the main part of our paper.

Key words: HPV, Cervical cancer, Ethical Issues

Background: Human papilloma virus (HPV) is common in human. Among more than 100 different types of HPV all are not health threatening. Some cause common condylomas and others plantar warts, but there is a group of HPVs that mainly infects the mucous epithelium of the anogenital tract and has an oncogenic nature¹.

Cervical cancer is the fourth most frequent cancer in women in the world and in 2012 there were approximately 530,000 new cases which represented 7.5% of all female cancer deaths and around 270,000 people die from Human Papilloma Virus (HPV) infection every year^{2,3}.

The incidence is highest in developing countries. The main reasons behind this situation are lack of resources in secondary prevention and treatment of the disease and poor sex education of the population^{2,3,4,5}. According to World Health Organization (WHO) sexually transmitted Human Papilloma Virus (HPV) is one of the major causes of cervical cancer. Two HPV strains (16 and 18) cause 70% of cervical cancers and precancerous cervical lesions. Cervical cancer (CC) is one of the top five cancers that affect women around the world⁶.

The pharmaceutical company Merck produces Gardasil, which prevents infection caused by certain strains of HPV. The Food and Drug Administration (FDA) approved a Gardasil as a vaccine for women in June 2006. Gardasil prevents two strains (16 and 18) of HPV which cause most cases of cervical cancer⁷.

The HPV vaccine is effective, if it is delivered before exposure to the virus, and preferably, at the pre-pubertal stage of a woman's life because the antibody responses are higher compared to those of after puberty⁸. The lifetime risk of cervical cancer can reduce by 44% among 70% of the pre-adolescent girls (girls below age 12) who are vaccinated against HPV⁹. The common side effects the vaccine have been mainly local reactions. In rare cases more severe signs or symptoms were found¹⁰. Moreover it is very important that the vaccine is has a 100% efficient to prevent precancerous lesions caused by the viral genotypes included in the vaccine¹¹.

Though an ethical dilemma lies in the balance of personal autonomy and choice and the protection of the population from the risk, vaccinations are counted as one of greatest achievements public health. From an epidemiological point of view, due to achieve protection against human papilloma virus (HPV) infection and potential development of cervical cancer among women. HPV vaccine is widely accepted even though it may lead to the neglect of other preventive strategies against cervical cancer⁶.

Policy decisions could be evaluated through several ethical theories. Utilitarianism, natural law theory via the Principle of Double Effect, and Principlism are common among the theories which are used; brief discussions of Religious Ethics and other possible approaches are added because of the criteria of the policy questions. Zikkerman (2006) did a striking analysis that applies ethical theories, such as utilitarianism, rule of double effect and principlism are needed for policy considerations. It was reported from the analyses that HPV vaccination can be recommended universally, including at ages 11–12 years¹². Bioethicists, who generally hold the values of patient autonomy and informed consent to be dominant, were doubtful about the reinforcement of vaccination. Some of them were worried about making HPV vaccination mandatory and some also opposed it. Compulsory vaccination encompasses the question, if achieving a higher level of coverage justifies the violation on parental autonomy¹³.

Cervical Cancer and Its Prevalence: Among the cancers of women in the world Cervical cancer (CC) is found in the top five. International Agency for Research on Cancer (IARC) revealed, in 2008 there were 530,000 new cases of cervical cancer worldwide, among these cases 85% were in developing countries¹³. Approximately 47, 000 new cases of cervical cancer and 223,000 deaths occurred in the year 2000^{15,16}. Though the incidence differs in different localities it is the most common gynecological cancer in developing countries^{15,17}. In India and Bangladesh 21-23% of female cancer is reported to be cervical cancer^{16,18,19,20}. In the developing countries the lack of consciousness is one of the most common reason of the death from this fatal cancer. According to World Health Organization statistics, incidence of cervical cancer cases in Bangladesh has been estimated 167 per 100,000 populations and 6,582 women die in the country from this cancer^{21,22}.

The development of Cervical Cancer, anogenital cancers, and oropharyngeal cancers are related with HPV types 16 and 18^{23,24}. According to WHO Cervical cancer is caused by sexually transmitted HPV²⁶. The other risk factors associated with cervical cancer are sexual orientation before the age of 16 years, monogamy, history of sexually transmitted diseases (HIV, HSV-2, genital wart etc), high parity, black race, smoking, low socio-economic status, lack of hygiene and oral contraceptive use²⁷.

In 2006, the FDA approved the HPV Vaccine Gardasil (against HR HPV types 16 and 18 as well as low-risk types 6 and 11) for all females aged 9 through 26. In 2009, the FDA also approved the use of this vaccine in males aged 9 through^{23,25}.

The high income countries have been succeeded to prevent the disease with prophylactic immunization and secondary prevention^{28,29}.

The Human Papilloma Virus (HPV) vaccine has recently been introduced (2016)for the first time in Bangladesh by the Ministry of Health and Family Welfare (MOHFW), with support from the Global Alliance for Vaccines and Immunizations (GAVI). This new vaccine introduction programme will run for two years in Gazipur district and if it is successful, GAVI will provide support for national introduction of HPV vaccine³⁰.

Ethical issues in HPV vaccination: Like any other vaccines in case of HPV vaccine ethical issues are important to understand, which is sometimes context specific. It is important to review the dynamics of ethics and HPV vaccine. In recent years several countries has introduced HPV vaccine in their national program²⁶. A new round of polarizing debates are started up with the steps taken to make the vaccine mandatory. Some religious conservatives were worried and they thought that the availability of a vaccine against a sexually transmitted disease would threaten abstinence-based prevention messages before the vaccine was licensed, this concern created argument for the vaccine. Abstinence is one of the approaches to HIV prevention taken by the Physician organization. Preventive measures include abstinence-based prevention massages like counseling adolescents and their families for being more responsible on sexual decision making including abstinence³¹. Some religious conservatives thought that the availability of the vaccine could affect the promotion of these messages. Some Advocacy groups agreed availability of the vaccine, but

they remain did not agree on making the vaccine mandatory. Their perspective was this decision of the state may lead to force a child to undergo an intervention that may be incompatible with her family's religious values and beliefs¹³.

The producers of the HPV vaccines were also included in the ethical controversy. The expense is huge for the research to introduce a successful product in the market. A balance in safety and efficacy is essential for successful programs. Continuous research maintains the chain of new usable products. Vigorous monitoring will record the success and failure of these programs globally. The reasonable aspects for HPV vaccine recommendation to people are more important than the ethical issues with any type of vaccination program³². But we cannot completely avoid the ethical issues while recommending HPV vaccine in a national immunization program of any country.

Holman compiled the different barriers to the vaccine. These barriers were stated by physicians and parents. Physicians cite financial concerns and parental attitudes and concerns, while most parents expressed the desire for more information about the vaccine before they agree to vaccinate their children³³. Whether the vaccine is advisable or not of the universal vaccination program, it is the basic right of the parents to decide about the sex education for their children, so all the information regarding the HPV vaccine must be provided to the parents⁵. If the parents consider the vaccine inappropriate for their daughters they must have the right to refuse to vaccinate their daughters. The ultimate decision on vaccinate the children should be taken by their parents to ensure parental autonomy^{34,35,36}.

Conclusion: In summary, it can be said from the above discussion that proposing a universal HPV vaccination campaign in girls and young women does not entail any particular ethical difficulties, providing that the above mentioned premises are taken into account. However as Government of Bangladesh has started a two years piloting program of HPV vaccination in 4 sub-districts (upazilas) of Gazipur district before scaling up the vaccine in national immunization program, it is very important to document the issues and ethical challenges which might raise concerns among parents and community and also to develop and examine innovative strategies to reduce the dilemma and address the unanswered questions related with ethical issues of HPV vaccination in local context.

References:

1. Molijn A, Kleter B, Quint W, van Doorn LJ. Molecular diagnosis of human papillomavirus (HPV) infections. *Journal of Clinical Virology*. 2005 Mar 31;32:43-51.y
2. Human papilloma virus (HPV) and cervical cancer [Internet]. World Health Organization. 2017 [cited 14 December 2017]. Available from: <http://www.who.int/mediacentre/factsheets/fs380/en/>
3. Lacey CJ, Lowndes CM, Shah KV. Burden and management of non-cancerous HPV-related conditions: HPV-6/11 disease. *Vaccine*. 2006 Aug 21;24:S35-41.
4. Yang BH, Bray FI, Parkin DM, Sellors JW, Zhang ZF. Cervical cancer as a priority for prevention in different world regions: an evaluation using years of life lost. *International journal of cancer*. 2004 Apr 10;109(3):418-24.
5. Ferlay J. (GLOBOCAN 2002) Cancer incidence, mortality and prevalence worldwide. IARC Cancer Base No. 5, version 2.0. <http://www-depdb.iarc.fr/globocan/GLOBOframe.htm>. 2004 Oct.
6. Navarro-Illana P, Aznar J, Díez-Domingo J. Ethical considerations of universal vaccination against human papilloma virus. *BMC medical ethics*. 2014 Apr 7;15(1):29.
7. Walter CS. Ethical, Legal, and Economic Considerations Related to the Mandatory Administration of the Human Papilloma virus Vaccine. *Notre Dame JL Ethics & Pub. Pol'y*. 2013;27:611.
8. Ilter E, Celik A, Haliloglu B, Unlugedik E, Midi A, Gunduz T, Ozekici U. Women's knowledge of Pap smear test and human papillomavirus: acceptance of HPV vaccination to themselves and their daughters in an Islamic society. *International Journal of Gynecological Cancer*. 2010 Aug 1;20(6):1058-62.
9. Diaz M, Kim JJ, Albero G, De Sanjosé S, Clifford G, Bosch FX, Goldie SJ. Health and economic impact of HPV 16 and 18 vaccination and cervical cancer screening in India. *British journal of cancer*. 2008 Jul 22;99(2):230-8.
10. Cortés J, Martínón F, Ferret G, Garcia E, Ramón JM, Garrido R, Miranda P, Dexeus D, Gil A, Cisterna R. Vacunasfrente al virus del papilomahumano: actualizacion. *Clínica e Investigación en Ginecología y Obstetricia*. 2010 Apr 30;37(2):63-74.
11. Garland SM, Hernandez-Avila M, Wheeler CM, Perez G, Harper DM, Leodolter S, Tang GW, Ferris DG, Steben M, Bryan J, Taddeo FJ. Quadrivalent vaccine against human papilloma virus to prevent anogenital diseases. *New England Journal of Medicine*. 2007 May 10;356(19):1928-43.
12. Zimmerman RK. Ethical analysis of HPV vaccine policy options. *Vaccine*. 2006 May 29;24(22):4812-20.
13. Colgrove J. The ethics and politics of compulsory HPV vaccination. *New England Journal of Medicine*. 2006 Dec 7;355(23):2389-91.
14. Blackman E, Thurman N, Halliday D, Butler R, Francis D, Joseph M, Thompson J, Akers A, Andraos-Selim C, Bondzi C, Taioli E. Multicenter study of human papilloma virus and

- the human papillomavirus vaccine: knowledge and attitudes among people of African descent. *Infectious diseases in obstetrics and gynecology*. 2013 Jul 16;2013.
15. Parkin DM, Bray FI, Devesa SS. Cancer burden in the year 2000. The global picture. *European journal of cancer*. 2001 Sep 30;37:4-66.
 16. Sultana R, Sultana N. Clinical profile and treatment protocol of invasive carcinoma of cervix. *Bangladesh Medical Journal Khulna*. 2013 Feb 3;45(1-2):11-4.
 17. Kulkarni PV, Jaiswal SS, Rathod SB, Khalique A, Kulkarni RR. Profile of malignancies at Medical College, Ambajogai--(15 years retrospective study). *Indian journal of cancer*. 1996 Mar;33(1):31-6.
 18. Banerjee AK, Bhattacharya N, Chowdhury MK, Chattopadhyay R, Sengupta J. Incidence of malignancy in Bankura (a retrospective study). *Journal of the Indian Medical association*. 1994 Dec;92(12):400-2.
 19. Sharma RG, Ajmera R, Saxena O. Cancer profile in eastern Rajasthan. *Indian journal of cancer*. 1994 Sep;31(3):160-73.
 20. Huq SF. Common cancers in Bangladesh: their trends through last three decades. *Bangladesh Med J*. 1988;17(3):5563.
 21. Papri FS, Khanam Z, Islam F, Hakim MM. Knowledge and Awareness About Risk Factors of Cervical Cancer, Its Screening and Vaccination Among the Women Attending Chittagong Medical College Hospital. *ChattagramMaa-O-Shishu Hospital Medical College Journal*. 2015 Nov 16;14(2):57-60.
 22. Khatun SF, Homaira R, Khatun S, Sharmin F et al Performance of VIA(Visual Inspection With Acetic Acid)and Colposcopic Biopsy as a Method Of Screening In Detecting Preinvasion and Early Cancerous Lesionof the Cervix.*Medicine Today*.2011;23(1):13-14
 23. Carter JR, Ding Z, Rose BR. HPV infection and cervical disease: a review. *Australian and New Zealand Journal of Obstetrics and Gynaecology*. 2011 Apr 1;51(2):103-8.
 24. C.C.R.Ragin,E.Taioli,J.L.Weissfeldetal.,“11q13amplificationstatus and human Papilloma virus in relation to p16 expression defines two distinct etiologies of head and neck tumours,” *British Journal of Cancer* ,vol.95,no.10,pp.1432–1438,2006
 25. FDA, “FDA Approves New Indication for Gardasil to PreventGenital Warts inMenandBoys,”Bethesda,Md,USA,2009,<http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2009/ucm187003.htm>.
 26. Human papillomavirus (HPV) and cervical cancer [Internet]. World Health Organization. 2017[cited 25 September 2017]. Available from: <http://www.who.int/mediacentre/factsheets/fs380/en/>
 27. Guner H, Taskiran C. Cervical cancer epidemiology and human papilloma virus. *Turkish J GynecolOncol*. 2007;4:11-9.
 28. Demarteau MN, Breuer T, Standaert B. Selecting a mix of prevention strategies against cervical cancer for maximum efficiency with an optimization program. *Pharmacoeconomics*. 2012 Apr 1;30(4):337-53.

29. Gakidou E, Nordhagen S, Obermeyer Z. Coverage of cervical cancer screening in 57 countries: low average levels and large inequalities. *PLoS Med.* 2008 Jun 17;5(6):e132.
30. HPV vaccine introduced in Bangladesh [Internet]. South-East Asia Regional Office. 2017 [cited 25 September 2017]. Available from: <http://www.searo.who.int/bangladesh/HPVvaccinelaunch/en/>
31. Post SG, Botkin JR. Adolescents and AIDS prevention: The pediatrician's role. *Clinical pediatrics.* 1995 Jan;34(1):41-5.
32. White MD. Pros, cons, and ethics of HPV vaccine in teens—Why such controversy? *Translational andrology and urology.* 2014 Dec;3(4):429.
33. Holman DM, Benard V, Roland KB, Watson M, Liddon N, Stokley S. Barriers to human papillomavirus vaccination among US adolescents: a systematic review of the literature. *JAMA pediatrics.* 2014 Jan 1;168(1):76-82.
34. Javitt G, Berkowitz D, Gostin LO: Assessing mandatory HPV vaccination: who should call the shots? *J Law Med Ethics.* 2008, 36:384–395.
35. Horn L, Howards C, Waller J, Ferris DG: Opinions of parents about schoolentry mandates for the human papillomavirus vaccine. *J Low Genit Tract Dis* 2010, 14:43–48.
36. Sussman AL, Helitzer D, Sanders M, Urquieta B, Salvador M, Ndiaye K: HPV and cervical cancer prevention counseling with younger adolescents: implications for primary care. *Ann Fam Med* 2007, 5(4):298–304.

Author Declaration: Fariha Haseen conceived the idea, conducted literature review, and developed the manuscript. Sadia Akther Sony conducted literature review and contributed in the development of the manuscript.

Conflict of Interest: Author declared n conflict of interest.