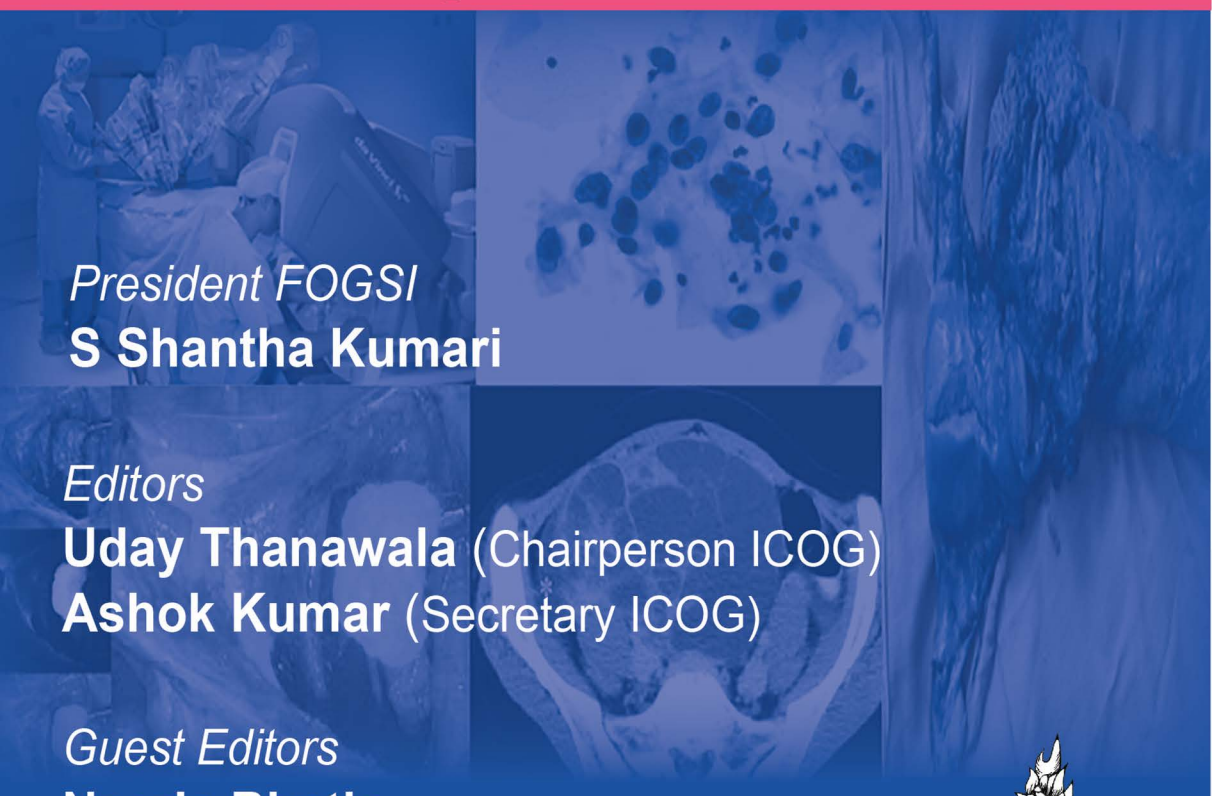
ks, visit our website www.jaypeebrothers.com, for detailed information on obstetrics & gynecology books, visit our website www.jaypeebrothers.com

Indian College of
Obstetricians & Gynaecologists

ICOG – Campus

Number 3 | June 2022 | www.icogonline.org

Gynecological Cancers
Recent Developments and Current Practice



President FOGSI
S Shantha Kumari

Editors
Uday Thanawala (Chairperson ICOG)
Ashok Kumar (Secretary ICOG)

Guest Editors
Neerja Bhatla
Seema Singhal

JAYPEE

Contents

1. **Cervical Cancer Journey over the Last Decade 1**
   Neerja Bhatla, Romey Rai, Seema Singhal
2. **Human Papillomavirus Vaccination: What's New? 16**
   Krishnendu Gupta, Mukta Agarwal
3. **Cervical Cancer Elimination: Reach the Unreachable 21**
   Bhagyalaxmi Nayak, Jagannath Mishra
4. **Borderline Ovarian Tumors 28**
   Sarita Bhalerao, Somya Suman
5. **Role of Minimally Invasive Surgery in Gynecologic Oncology: Today and Tomorrow 35**
   Hafizur Rahman, Prasanna G
6. **Role of Tumor Markers in Diagnosis and Management 45**
   Kavita N Singh, Kirti Patel, Sonal Sahni, Nehal Singh
7. **Imaging in Gynecologic Malignancies 52**
   Ekta Dhamija
8. **Genetic Testing in Gynecologic Oncology: When, How, and What? 61**
   Shalini Rajaram, Ipshita Sahoo
9. **Palliative Care in Gynecologic Oncology: Widening the Horizons 71**
   Sushma Bhatnagar, Raghav Gupta

Index 81

Chapter 2

Human Papillomavirus Vaccination: What's New?

Krishnendu Gupta, Mukta Agarwal

INTRODUCTION

Human papillomaviruses (HPVs) are double-stranded DNA viruses that infect squamous cells that cause proliferative lesions such as skin wart. These viruses are classified by genotype—130 genotypes have been identified based on L1 capsid protein.[1] These viruses show predilection for causing infection of cutaneous or mucosal surfaces.[1] They are classified into high- and low-risk groups based on their oncogenic potential. 100% cervical cancers are associated with HPV infection out of which 50–70% caused by HPV 16, 7–20% are caused by HPV 18.[1] HPV is also associated with vulval, vaginal, anal, and head and neck cancers.

Cervical cytology screening is very helpful in preventing cervical carcinoma in many developed countries.[1] World Health Organization (WHO) guideline recommends HPV testing in cervical cancer screening. Many countries have established cytology-based screening program but scientific studies suggest that HPV testing is superior to cytology-based screening programs.[2]

All preteens need HPV vaccination to remain protected from cancer later in the life. HPV vaccination is suggested at age 11–12 years. WHO recommends that primary target for HPV vaccination is girls aged 9–14 years, ideal before sexual debut.[3]

For girls <15 years of age, a two-dose schedule which is 6 months apart is advised, with maximal duration between the doses preferably not >15 months. If second dose is given in an interval shorter than 5 months from the first dose, it is recommended to administer a dose at least 6 months from the first dose.[3]

Even though efficacy of the vaccine reduces for girls >15 years, a three-dose schedule is advised, at 0, 2, and 6 months.[3] Three doses are also recommended for immunocompromised individuals <15 years of age. However, a recent Indian study recommended the use of two-dose schedule in girls from 15 to 18 years.[4]

Vaccination is not recommended for everyone above age of 26 years as these women have already had exposure to HPV infection.[3] Though, benefit is not guaranteed, HPV vaccine can be given after the age of 26 years.

JAYPEE BROTHERS

CONTRAINDICATIONS OF HUMAN PAPILLOMAVIRUS VACCINE[5]

- Any person with known hypersensitivity/allergic reaction to any ingredient of HPV vaccine[3]
- Allergy to yeast (Gardasil 4 and Gardasil 9)[3]
- Pregnancy[4]
- People who are moderate to severely ill need to wait for vaccination till they get better.[3]

TYPES OF HUMAN PAPILLOMAVIRUS VACCINE

Currently, there are three types of HPV vaccines available:[5]

- *Nonavalent HPV vaccine*: Gardasil 9
- *Quadrivalent HPV vaccine*: Gardasil 4
- *Bivalent HPV vaccine*: Cervarix

All the three vaccines protect against HPV 16 and 18. In addition, Gardasil 4 also protects against HPV 6 and 11; Gardasil 9 has the widest range of coverage and protects against HPV 6, 11, 16, 18, 31, 33, 45, 52, and 58.[3] Cervarix being a bivalent vaccination directed only against HPV 16 and 18 does not protect against HPV 6 and 11.[6]

Ongoing research to manufacture second-generation prophylactic HPV vaccines are currently being clinically evaluated using alternative viral components (capsomere or minor capsid HPV L2 protein) and incorporating more cost-effective strategies. In addition, major pharmaceutical companies worldwide, including India (Serum Institute of India: SII, Zydus Cadila), are in the process of manufacturing the first-generation HPV vaccines at a much lower cost. The quadrivalent vaccine from SII is expected to be marketed for commercial use in 2022.

NEW RECOMMENDATIONS

The 4–7 April 2022 convening of WHO Strategic Advisory Group of Experts on immunization (SAGE) evaluated the evidence derived over past few years that single-dose schedules of HPV vaccine provide comparable efficacy to the two or three dose regimens.[7] This could be a turning point in preventing cervical cancer as more doses will reach to more girls.[7]

More than 95% cervical cancers are caused by sexually transmitted HPV which is fourth most common cancer in women globally with most of them living in low- or middle-income countries.[7] Most of the infections clear out within 2 years and do not result in disease or cancer,[8] but persistent infections may cause cervical cancer.

SAGE urged all countries to provide HPV vaccine and prioritize multiage cohort catch up missed and old girls. This will lead to more girls and women

JAYPEE BROTHERS

to be vaccinated and thus preventing them from having cervical cancer in future.[7]

SAGE recommendation for HPV vaccine is as follows:[7]

- *One or two-dose schedule* for the primary target of girls aged *9–14* years
- *One or two-dose schedule* for young women aged *15–20* years
- Two doses with a 6-month interval for women *older than 21* years.

Immunocompromised individuals must receive at least three doses if feasible, there is lack of evidence for efficacy on single dose in this group.[7]

Globally, the coverage of vaccine is still very low. In 2020, the global coverage with two-dose vaccine was only 13%.[7]

There are several factors influencing this which includes supply challenges, programmatic challenges, and cost of delivering two doses to older girls who are not part of childhood vaccination programs.[7]

Institutions, local organizations, nongovernmental organizations (NGOs) such as Rotary International[9] amongst numerous others can implement successful HPV vaccination. Adequate planning and resources that support information sharing and mobilization are essential. These results may lead to successful development of programs and policies related to HPV vaccination in low- and middle-income countries.[10]

Single dose of vaccine is less costly, less resource intensive, and easier to administer. It facilitates implementing catch up campaigns for multiage groups, reduces challenges linked to tracing girls for second dose.[7]

SIDE EFFECTS

The common side effects following HPV vaccination include pain, redness, and/or swelling around the area of the arm where the shot was given; rarely, there could be a feeling of dizziness or fainting, headache, or feeling tired, nausea, muscle, or joint pain.[3,11]

CURRENT RECOMMENDATIONS

Although there are numerous guidelines and recommendations by various international federations and health organizations, the current recommendations, and conclusions on HPV vaccination by the American College of Obstetricians and Gynecologists (ACOG) Committee Opinion Number 809 is an excellent and comprehensive read.[12] The 12 recommendations are as follows:

- The Advisory Committee on Immunization Practices and ACOG recommend routine HPV vaccination for girls and boys at the target age of 11–12 years (but it may be given from the age of 9 years) as part of the adolescent immunization platform.
- HPV vaccination should be strongly recommended to eligible girls.

JAYPEE BROTHERS

- All adolescent girls and young women be vaccinated with the HPV vaccine during the catch-up period (ages 13–26 years), regardless of prior exposure to HPV, sexual activity, or sexual orientation.
- For older women aged 27–45 years who are previously unvaccinated, a shared clinical decision-making be used, after explaining the patient's risk for acquisition of a new HPV infection and limited efficacy of vaccine.
- ACOG does not recommend giving nonavalent vaccine to those who are already vaccinated using bivalent or quadrivalent vaccine.
- HPV vaccination is recommended for women above 26 years of age even if the HPV screening test is positive.
- There is no need to test for HPV DNA prior to vaccination in older women.
- HPV vaccination is not recommended during pregnancy; and a routine pregnancy test is not mandatory prior to vaccination.
- The HPV vaccine can be given during lactation.
- In children with a history of sexual abuse or assault, the HPV vaccine should be given as early as possible, starting at age 9 years. HPV vaccination is also recommended in victims of sexual abuse, preferably at the time of clinical examination itself. Same recommendations are followed for patients with abnormal cervical screening results, but decreased efficacy and importance of follow-up should be emphasized.[12]

The HPV vaccines are among the most effective vaccines available worldwide, with data demonstrating >99% efficacy when administered to HPV naïve women.[12]

The major challenges currently faced in the low- and low middle-income countries in promoting HPV vaccination (being currently expensive compared to other vaccines, logistical issues to recall adolescent girls for the second and/or third dose, the after-effects global crisis of vaccine supply due to the COVID-19 pandemic) will hopefully be greatly reduced to a great extent once the single-dose HPV vaccination is made official for use in adolescent girls. We are all waiting with bated breath for this much-awaited announcement which will definitely accelerate the global strategy of WHO to reduce and finally eliminate cervical cancer.

KEY MESSAGES

- Cervical cancer can be safely and effectively prevented by HPV vaccination.
- Cervarix and Gardasil are first-generation vaccines, and nonavalent Gardasil-9 is the new second generation vaccine.
- All girls between 9 and 14 years are advised two-dose vaccination schedule and for >15 years a three-dose schedule is currently recommended.
- Women between 26 and 45 years may be counseled regarding decreased HPV vaccine at this age but it may be given on case-to-case basis.
- Recent evidence suggests that single-dose schedule is effective and may make widespread coverage possible, but further studies required.

JAYPEE BROTHERS

REFERENCES

1. Stanley M. Pathology and epidemiology of HPV infection in females. Gynecol Oncol. 2010;117(2):S5–10.
2. Salud OP de la. Integrating HPV testing in cervical cancer screening program: a manual for program managers PAHO; 2016. [online] Available from: https://iris.paho.org/handle/10665.2/31393. [Last accessed May 2022].
3. Centers for Disease Control and Prevention. (2022). HPV Vaccination: What Everyone Should Know. [online] Available from: https://www.cdc.gov/vaccines/vpd/hpv/public/index.html. [Last accessed May 2022].
4. Arora M, Lakshmi R. Vaccines - safety in pregnancy. Best Pract Res Clin Obstet Gynaecol. 2021;76:23-40.
5. Bergman H, Buckley BS, Villanueva G, Petkovic J, Garritty C, Lutje V, et al. Comparison of different human papillomavirus (HPV) vaccine types and dose schedules for prevention of HPV-related disease in females and males. Cochrane Gynaecological, Neuro-oncology and Orphan Cancer Group, editor. Cochrane Database Syst Rev. 2019;2019(11):CD013479.
6. Nicol AF, de Andrade CV, Russomano FB, Rodrigues LS, Barreto AS, Santos CNO, et al. HPV vaccines: their pathology-based discovery, benefits, and adverse effects. Ann Diagn Pathol. 2015;19(6):418-22.
7. World Health Organization. One-dose Human Papillomavirus (HPV) vaccine offers solid protection against cervical cancer. [online] Available from: https://www.who.int/news/item/11-04-2022-one-dose-human-papillomavirus-(hpv)-vaccine-offers-solid-protection-against-cervical-cancer. [Last accessed May 2022].
8. Dunne EF, Park IU. HPV and HPV-associated diseases. Infect Dis Clin North Am. 2013;27(4):765-78.
9. Mandal R, Banerjee D, Gupta K, Chatterjee P, Vernekar M, Ray C. Experience of human papillomavirus vaccination project in a community set up – An Indian Study. Asia Pac J Cancer Prev. 2021;22(3):699-704.
10. Ladner J, Besson MH, Audureau E, Rodrigues M, Saba J. Experiences and lessons learned from 29 HPV vaccination programs implemented in 19 low and middle-income countries, 2009-2014. BMC Health Serv Res. 2016;16(1):575.
11. Gonçalves AK, Cobucci RN, Rodrigues HM, de Melo AG, Giraldo PC. Safety, tolerability and side effects of human papillomavirus vaccines: a systematic quantitative review. Braz J Infect Dis. 2014;18(6):651-9.
12. American College of Obstetricians and Gynecologists' Committee on Adolescent Health Care, American College of Obstetricians and Gynecologists' Immunization, Infectious Disease, and Public Health Preparedness Expert Work Group. ACOG Committee Opinion 809. Human Papillomavirus Vaccination. Obstet Gynecol. 2020;136(2):e15-21.

JAYPEE BROTHERS

for detailed information on obstetrics & gynecology books, visit our website www.jaypeebrothers.com, for detailed information on obstetrics & gynecol

ICOG – Campus

Gynecological Cancers

Recent Developments and Current Practice

Gynecological cancers are on the rise and are now encountered routinely in all clinics. These patients may present at any age, depending on the type of tumor they have. Thus a working knowledge of the management of gynecological cancers is essential in today's world. Moreover, great strides have been made by science and technology that have increased the scope of prevention, investigation and treatment. Even palliative care has developed into a specialized system that allows for personalized care, dignity and comfort at all stages of the disease. Ob-Gyn specialists who care for these women require a resource that covers a range of issues in depth and breadth if they are to provide comprehensive care. This book offers a rich resource of material presented in a stimulating style. It maintains the practical multidisciplinary approach that encompasses both preventive and therapeutic aspects, providing expert, practical, person-centered, evidence-based overview of recent advances in the field of gynecological cancers for practitioners, researchers and students who need updated information for understanding and treating gynecological cancers.

Printed in India

Available at all medical bookstores
or buy online at www.jaypeebrothers.com



JAYPEE BROTHERS
Medical Publishers (P) Ltd.
EMCA House, 23/23-B, Ansari Road,
Daryaganj, New Delhi - 110 002, INDIA
www.jaypeebrothers.com

Join us on facebook.com/JaypeeMedicalPublishers

Shelving Recommendation
OBSTETRICS & GYNECOLOGY

