AOGD BULLETIN

Volume 22 I October 2022 I Monthly Issue 6

Safeguarding women and their Doctors

Issue Theme:
Cancer Cervix "The Silent Killer"

AOGD SECRETARIAT

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AOGD Bulletin

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Foreword

Latest issue of AOGD monthly bulletin is devoted to various topics in cancer cervix. All the articles have been contributed by leading Gynae oncologist from the city. This issue of AOGD bulletin updates knowledge about burning topics in cancer cervix. Latest knowledge about HPV vaccination, current concepts in the management of advanced and recurrent disease have been highlighted. Globally WHO and other international agencies are targeting elimination of cancer cervix by 2030 and have highlighted a practical approach for this goal.

In India we need to put all our efforts together by involving gynaecologists, general physicians, nurses, and paramedical persons to achieve a goal of 50% reduction in cases of cancer cervix by 2025. India contributes to 20-25% new cases of cancer cervix and equal number of deaths due to cancer cervix every year. We need a mass campaign on the lines of previous health initiatives to achieve this.

I am sure readers will find the present issue informative and useful.

Happy reading.

Dr Sunesh Kumar
Former Professor and Head
Department of Obstetrics & Gynaecology
A.I.I.M.S. , New Delhi

Senior Consultant- Gynae Oncology
Sitaram Bhartia Institute of Science and Research, New Delhi

From the AOGD Office


Dr. Asmita M. Rathore


Dr. Y. M. Mala


Dr. Deepti Goswami

Greetings to all our AOGD members.

The preparations for the 44th AOGD Conference is in full swing and the theme of the conference, "Quality Care for Women: Sharing Vision, Sharing Solutions" is very pertinent to the present situation of health care. The whole organizing team from Maulana Azad Medical College is working relentlessly to make the conference interesting, informative and a memorable experience. This year is special as a physical AOGD conference is happening after 2 years of Covid pandemic and hence has the advantage of direct interaction and exchange of knowledge and experiences with the invited national and international speakers. The scientific program of both conference and pre-conference workshops have been designed in such a way that various aspects of sub-specialities of obstetrics and gynecology will be covered.
It gives me immense pleasure to invite you all for the upcoming AOGD conference to be held on 12th and 13th November at the India Habitat Centre and make the conference a successful event.

The present bulletin is on cervical cancer and the editorial team has covered a very important aspect of prevention which includes HPV vaccination and various screening methods.

Wishing you all a very happy and a safe Diwali !

Dr. Asmita M Rathore, President
Dr. Y M Mala, Vice President
Dr. Deepti Goswami, Secretary

AOGD Risk Management Support [ARMS] Group

One of the ways to ensure the stress-free work environment and optimal patient care is mutual support among professional colleagues. We propose to form an advisory group of senior AOGD members that can be contacted if one of us is caught in a complex clinical dilemma / dealing with aggressive clients or is apprehensive about how to document or effectively troubleshoot a potential problem. This group will provide the timely advice and will be led by-

Convener- **Dr. Vijay Zutshi** - 9818319110

Co convener- **Dr. Aruna Nigam** - 9868656051

We invite suggestions from all members regarding functioning of this cell which will guide us forming the SOPs. Any member interested in being part of Advisory group may contact the convener.

Pl mail to aogdmamc2022@gmail.com

From the Editor's Desk

Dr. Madhavi M. Gupta
Editor

Dr. Nalini Bala Pandey

Dr. Chetna A. Sethi

Dr. Reena Rani

Co-Editors

Greetings to all !

Dear Friends

The festival of lights is round the corner and we wish our readers a Deepawali filled with joy and light. It's been two years since we lighted diyas with fervour and everyone is eagerly looking forward to the same.

The editorial team is pleased to present to you the October issue of the AOGD Bulletin.

It has been a long drawn wish to bring out a bulletin as an endeavour to promote preventive strategies for the 'Silent Killer'. As we move on along the path from therapy to prevention and now a global initiative for elimination, we dedicate this issue to the cause of cancer cervix.

In the Game Changer section we bring to you the WHO Strategic Advisory Group of Experts on Immunization (SAGE) recommendation on revised dosing schedule for the HPV vaccine and the research behind it which brings to light that single dose HPV Vaccine provides solid protection and has the potential to further set stage for cervical cancer elimination. The two studies include the Indian study on Vaccine Efficacy on HPV infection after one, two and three doses and The HPV Vaccine Trial in Costa Rica.

HPV Vaccine was a step forward in preventing cancer cervix and we have come a long way. Dr Neerja Bhatla, who has been a key figure in the research leading to the development of this vaccine has covered the journey of HPV vaccine and what the future research holds. Concerted efforts at all fronts are required for including HPV vaccine in the universal immunization programme of India.

It is not only India that cancer cervix has been creating havoc, the world is it's stage. Global strategies are much needed to check this killer. Authors Dr Sweta Balani and Dr Sonal Bathla provide an insight into the bottle necks present and how global cancer elimination initiatives can achieve its targets by 2030 following the 90-70-90 path towards cervical cancer elimination.

Radiotherapy and surgery are the cornerstone of managing cancer cervix. Treatment options in advanced disease are limited and with the success of target therapy in other solid tumours there is interest and new research in applying the same to cancer cervix. Dr Amita Suneja has explained the difference between target therapy and immunotherapy and the principles and benefits of the same and covered different therapy options available & being researched.

Pregnancy is an opportune time for cervical cancer screening in India, when a woman approaches the health care system for the first and occasionally the last time. Dr Nilanchali Singh has dealt with this problem raising it's head during pregnancy, both precancer stage and a full blown cancer.

Risk Management under 'Safeguarding the Doctors' section is dedicated to Documentation. The relevance of complete documentation can never be overstated, the only document which stands by you in the court of Law. The author walks us through it's nuances covering, both clinical and non-clinical documentation, guidelines on documentation by the National Medical Commission, along with discussing the access, disclosure and confidentiality aspects. What all needs to be documented and how to do it will help each one of us in our patient interactions. Dr S N Basu has covered all about this important part of our medical practice.

My heartfelt gratitude to all the authors for their efforts in putting together an article for keeps.

As always, we look forward to receive your feedback to help us bring out a better version each time.

Yours in health

Dr. Madhavi M Gupta
Editor

44th Annual AOGD Conference

12th & 13th November, 2022 | India Habitat Center, New Delhi

Association of Obstetricians and Gynaecologists of Delhi

Organized by: Department of Obstetrics & Gynaecology,
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- Endoscopy in Obs. & Gynae
- Gynae Oncology
- Miscellaneous

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AOGD 2022 Pre-Conference Workshops

9th November, 2022

Workshop	Time	Venue	Convener	Co- Convener
Hands on Workshop - Basic ultrasound skills for Obstetricians	10:00am-5:00pm	Department of Fetal Medicine , Rainbow Children Hospital, Malviya Nagar	Dr. Seema Thakur Dr. Chanchal	
A to Z of PPH	9:00am – 3:30pm	New ground floor lecture theater, Maulana Azad Medical College & LNH	Dr. Shashi Lata Kabra Dr. Shakun Tyagi	
Revise the Basics, Enhance the Skills. Cervical Cancer - Prevention and Screening	9:00am-3:00pm	Auditorium, Sir Ganga Ram Hospital	Dr. Mrinalini Mani Dr. Meenakshi Ahuja	Dr. Pinkee Saxena Dr. Divya Singhal

10th November, 2022

Workshop	Time	Venue	Convener	Co- Convener
Gynae Endoscopy: Rejuvenating Young Minds	9:00am - 5:00pm	Board Room, Director's wing, All India Institute of Medical Sciences	Dr. Neerja Bhatla Dr. Neena Malhotra	Dr. Garima Kachhawa Dr. Reeta Mahey
Optimizing emergency obstetric care. Point of care'- (POC) assessment and intervention	9:00am- 4:00pm	Lady Hardinge Medical College & SSKH	Dr. Reena Yadav Dr. Manju Puri	Dr. Ratna Biswas Dr. Swati Agrawal
Learn IUI. Trouble shooting and new regulations	9:30am-4:00pm	Auditorium, Max Hospital, Saket,	Dr. Manju Khemani Dr. Sunita Arora	Dr. Madhu Goel Dr. Nishtha Jaiswal

11th November, 2022

Workshop	Time	Venue	Convener	Co- Convener
Maternal Resuscitation	9:00am -1:00pm	Skill lab Administrative Block, 3rd Floor, University College of Medical Sciences & GTBH	Dr. Amita Suneja Dr. Kiran Guleria	Dr. Archana Chaudhary Dr. Shruthi Bhaskaran
Demystifying Ovary	9:00am – 5:00pm	Jaypee Siddarth, Rajendra Place, New Delhi	Dr. Surveen Ghumman	Dr. Deepti Goswami
Anorectal Disorders: A Primer for the Gynaecologist	1:00pm – 6:00pm	Working women Auditorium, Sir Ganga Ram Hospital	Dr. Geeta Mediratta	Dr. Chandra Mansukhani Dr. Shrihari Anikhindi
Gynae Oncosurgery (Live workshop)	8:30am -4:00pm	Old LT, behind OPD building Vardhman Mahavir Medical College & SJH	Dr. Sunita Malik Dr. Saritha Shamsunder	Dr. Archana Mishra

Call for Nominations

AOGD President & Vice President Election (2023-24)
Call for nominations

Nominations are invited from eligible AOGD members for the following posts

- President (2023-24)
- Vice President (2023-24)

Last date for submission of nominations is 18th November 2022

- Applications by desirous candidates should be submitted on the prescribed form available on AOGD website (www.aogd.org) / bulletin / office, with due entry in the office register.
- The nomination shall be proposed by one regular member and seconded by two regular AOGD members.
- The candidate, his/her proposer and seconder should have cleared all their dues towards the membership subscription in full. Non compliance with this condition shall render the nomination invalid.
- Nominations as per the eligibility criteria should reach AOGD secretariat: Room no. OG -14, 1st Floor, PNW-1, department of Obst. & Gynae, Maulana Azad Medical College & Lok Nayak Hospital, New Delhi- 110002 (Phone no. 9211656757) by 18th November 2022.

Accepted nomination(s) will be displayed on AOGD website by 1st December 2022.

NOTE:

- The new members joining AOGD after the date of call for nominations willl not be eligible for voting.
- Associate members are not eligible to vote.

Dr. Deepti Goswami
(Secretary AOGD
9968604348)

Eligibility Criteria for PRESIDENT AOGD

1. He/she shall be a senior and active member of faculty in a multidisciplinary hospital of Delhi in the public or the private sector, with such hospital having clinical and para-clinical departments and having post graduate courses, duly recognized by the National Medical Commission and/or the National Board of Examination.
2. He/she must have held the post of professor/ senior consultant/an equivalent there of with such hospital for more than 10 years.
3. He/she must have the experience of having completed at least one tenure as the chairperson of a sub-committee of the AOGD or the experience of having completed at least one tenure as Vice President or Secretary or member of the Executive Committee of the AOGD.
4. He/she must be a life member of the AOGD with more than twenty years of experience after post graduation in the specialty of obstetrics and gynaecology.
5. He/she should have experience of conducting academic conferences, seminars or workshops.
6. A person who has held the post of President of the AOGD in the past shall be ineligible to hold the post of President of the AOGD again.
7. Faculty from the institution that fields the President shall be ineligible to apply for election to the post of President for a period of five years from the date of start of the tenure of that President.

Eligibility Criteria for VICE PRESIDENT AOGD

1. He/she shall be a senior member of faculty in a multidisciplinary hospital of Delhi in the public or the private sector, with such hospital having clinical and para-clinical departments and having post graduate courses, duly recognized by the National Medical Council / National Board of Examination.
2. He/she must have held the post of professor / senior consultant / or an equivalent thereof with such hospital for more than seven years.
3. He/she must have the experience of having completed at least one tenure as the chairperson of a sub-committee of the AOGD or the experience of having completed at least one tenure as Secretary or Treasurer or Editor or member of the Executive Committee of the AOGD having attended at least 75% of the meetings of the Executive Committee during his/her tenure as member of the Executive Committee
4. He/she must be a life member of the AOGD with more than fifteen years of experience after post graduation in the specialty of obstetrics and gynaecology.
5. He/she should preferably, have experience of conducting academic conferences, seminars or workshops.
6. A person who has held the post of Vice-President of the AOGD in the past shall be ineligible to hold the post of Vice- President of the AOGD again.

AOGD Subcommittees Chairperson Election (2023-25)
Call for nominations

Nominations are invited from eligible AOGD members for the post of chairperson of following subcommittees:

1. Endometriosis Sub-Committee
2. QI Obst & Gynae Practice Sub-Committee
3. Oncology Sub-Committee
4. Urogynaecology Sub-Committee
5. Adolescent Health Sub-Committee
6. Fetal Medicine & Genetics Sub-Committee
7. Endoscopy Sub-Committee

Last date for submission of nominations is 18th November 2022

Nominations as per the eligibility criteria should reach AOGD secretariat: Room no. OG -14, 1st Floor, PNW-1, department of Obst. & Gynae, Maulana Azad Medical College & Lok Nayak Hospital, New Delhi- 110002 (Phone no. 9211656757) by 18th November 2022.

Dr. Deepti Goswami
(Secretary AOGD)

Eligibility Criteria for AOGD Sub-committee chairperson

1. The chairperson of a sub-committee should have been a member of the sub-committee in question for at least one term, with one term being equivalent to two years, prior to his/her appointment as chairperson of that sub-committee.
2. He/she should have been a member of the AOGD for fifteen years.
3. He/she should have experience in the field related to the subcommittee.
4. He/she should have completed at least fifteen years from the date of his/her registration as a medical practitioner. Further, he/she should have held a senior / faculty position for not less than that of associate professor, senior consultant or an equivalent there of in his/her respective organization, for a period of at least five years .
5. No person should hold chairperson ship of the same subcommittee for two consecutive terms with each term comprising of two years. Further, a person who has been chairperson of one subcommittee cannot be nominated as chairperson of another subcommittee unless separated by a duration equivalent to two terms of the subcommittee.
6. The Executive Committee may lay down additional criteria for the eligibility and pre-requisites for appointment as chairperson of each sub-committee from time to time.
7. An eligible member must send an application for nomination as chairperson of a sub-committee stating therein his/her previous experience in the field related to the sub-committee and future vision for furthering the goals of the AOGD through such sub-committee. One person shall not apply for chairpersonship of more than one sub- committee at a time. The application shall be scrutinized by the Executive Committee of AOGD for nomination as chairperson.
8. In the event of more than one application being received for appointment as chairperson of a subcommittee, and in the absence of unanimous decision of the Executive committee in this regard, the Executive Committee shall decide the nomination by cast of secret ballot.
9. The tenure of the chairperson of subcommittee shall be for a period of two years.

The Association of Obstetricians & Gynaecologists of Delhi

Nomination Form

Name:_____

Designation:_____

AOGD Membership no:_____

Official Address:_____

Residential Address:_____

Phone:_____Email:_____

Bio Sketch (250words)

Post Applied for

President 2023-24 ☐ **Vice President** 2023-24 ☐ **Chairperson** 2023-2025 ☐

Name of Subcommittee

Proposed by – Name **AOGD Membership no.** **Signature**

1.

Seconded by

1.

2.

Nominations should reach at AOGD Office
For any Query please call Mrs. Sarita : 9211656757

GAME CHANGER:

SAGE Review: One-dose Human Papillomavirus (HPV) vaccine offers solid protection against cervical cancer, The Indian study on Vaccine Efficacy on HPV infection after one, two and three doses and The HPV Vaccine Trial in Costa Rica

Madhavi M Gupta*, Chetna A Sethi**
*Director Professor, **Specialist, Department of Obstetrics & Gynaecology, MAMC & Lok Nayak Hospital, Delhi

Abstract of the research articles are available free at the journal websites and on PubMed (http://www.ncbi. nlm.nih.gov/pubmed)

Cancer cervix is one of the most common cancer among women, with 90% of affected women living in low and middle income countries.[1]

Burden of disease in India: It is the 2nd most frequent cause of cancer among women in India and 2nd most frequent cancer among women between 15 and 44 years of age.[2] More than 123000 new cases and 77000 deaths occur annually with 83.2 % of invasive cervical cancers attributed to HPVs 16 and 18.[2]

Human papillomavirus (HPV) vaccines (bivalent, quadrivalent and nanovalent) with sero conversion rates of 93 to 100 percent are highly effective and prevent cervical disease, both CIN2 & 3 and adenocarcinoma in -situ. Cervical cancer still remains a major concern because of inequitable access and low population coverage in LMICs.

The recommended two and three dose HPV vaccine regimens are effective but have multiple logistical barriers more so in LMICs. A single dose regimen may prove to be a boon for vaccine coverage and help move faster towards Cervical Cancer Elimination Initiative, launched in 2020 with the goal 90 per cent vaccine coverage among girls of age 15, by 2030.

Single dose regimen will be cost effective, resource saving, easy to administer, have better acceptability and uptake across all age groups.

In a recent convening of the WHO Strategic Advisory Group of Experts on Immunization (SAGE) the available evidence for Single dose HPV vaccine was reviewed and recommendations made.

We also discuss two studies providing evidence for the efficacy of Single dose vaccine schedules in comparison to multi dose schedules.

SAGE review: One dose Human Papillomavirus(HPV) vaccine offers solid protection against cervical cancer.[3]

WHO Strategic Advisory Group of Experts on Immunization (SAGE) in a recent convening from April 4-7, 2022 evaluated the emerging data regarding the comparable efficacy of single-dose schedules to the multi dose regimens.

SAGE's review concluded that a single-dose HPV vaccine gives significant protection against virus that causes cervical cancer, and is comparable to multi dose schedules.

SAGE has recommended updating the dose schedule for HPV vaccination as follows:

- **one or two-doses** for girls aged **9-14 years (**primary target)
- **one or two-dose** for young women aged **15-20 years**
- **two doses** with a 6-month interval for women **older than 21 years**.

With limited available evidence for efficacy of a single dose vaccination in immunocompromised women, including those with HIV, they should receive three doses of the vaccine. If not feasible, at least two doses should be administered.

The Indian Study

Vaccine efficacy against persistent human papillomavirus (HPV) 16/18 infection at 10 years after one, two, and three doses of quadrivalent HPV vaccine in girls in India: a multicentre, prospective, cohort study

Basu P, Malvi SG, Joshi S, Bhatla N, Muwonge

R, Lucas E, Verma Y, Esmy PO, Poli URR, Shah A, Zomawia E, Pimple S, Jayant K, Hingmire S, Chiwate A, Divate U, Vashist S, Mishra G, Jadhav R, Siddiqi M, Sankaran S, Prabhu PR, Kannan TPRA, Varghese R, Shastri SS, Anantharaman D, Gheit T, Tommasino M, Sauvaget C, Pillai MR, Sankaranarayanan R.. Lancet Oncol. 2021 Nov;22(11):1518-1529. doi: 10.1016/S1470-2045(21)00453-8. Epub 2021 Oct 8. Erratum in: Lancet Oncol. 2022 Jan;23(1):e16. PMID: 34634254; PMCID: PMC8560643.

This study was initially rolled out as a randomised trial designed to compare three and two doses of quadrivalent human papillomavirus (HPV) vaccine in adolescent girls in India but was converted by default to a cohort study after suspension of HPV vaccination in trials by the Indian Government.

Subsequently, the aim of the cohort study was revised to compare vaccine efficacy of single dose to that of three and two doses in protecting against persistent HPV 16 and 18 infection at 10 years post vaccination.

HPV Vaccine: Quadrivalent HPV vaccine (Gardasil [Merck Sharp & Dohme, Whitehouse Station, NJ, USA]; 0·5 mL administered intramuscularly).

The planned protocol was to enroll 20,000 unmarried girls, aged 10-18 years, from 9 centers across India and randomly assigned to either two doses or three doses of the vaccine. The recruitment was initiated in September 2009 and was required to be stopped in April 2010 (as per the regulation by the Indian Government).

After suspension of recruitment and vaccination, the study became a longitudinal, prospective cohort study by default**.** At this point recruited participants (17,729 eligible girls) were allocated to four cohorts on the basis of the number of vaccine doses received per protocol: the two-dose cohort (received vaccine on days 1 and 180 or later), three-dose cohort (days 1, 60, and 180 or later), two-dose default cohort (days 1 and 60 or later), and the single-dose default cohort. Annual follow up was done and the cervical specimens were collected from participants 18 months after marriage or 6 months after first childbirth, whichever was earlier, for assessment of incident and persistent HPV infections. Married participants underwent screening for cervical cancer at 25 years of age. Age-matched unvaccinated women served as controls. Efficacy of vaccine against persistent HPV 16 and 18 infections (endpoint) was analysed for single-dose recipients and compared with two-dose and three-dose recipients.

In all, 4348 participants had three doses, 4980 had two doses (at 0 and 6 months), and 4949 had a single dose. Vaccine efficacy against persistent HPV 16 and 18 infection among participants evaluable for the endpoint was 95.4% (95% CI, 85.0 - 99.9) in the single-dose default cohort 93.1% (95% CI, 77.3 - 99.8) in the two-dose cohort , and 93.3% (95% CI, 77.5 - 99.7) in three-dose recipients; 2135, 1452, 1460 women were assessed respectively, in each cohort.

The authors interpreted that a single dose of HPV vaccine provides similar protection against persistent infection from HPV 16 and 18, the genotypes responsible for nearly 70% of cervical cancers, to that provided by two or three doses.

The HPV Vaccine Trial in Costa Rica (CVT):

Evaluation of Durability of a Single Dose of the Bivalent HPV Vaccine: The CVT Trial

Kreimer AR, Sampson JN, Porras C, Schiller JT, Kemp T, Herrero R, Wagner S, Boland J, Schussler J, Lowy DR, Chanock S, Roberson D, Sierra MS, Tsang SH, Schiffman M, Rodriguez AC, Cortes B, Gail MH, Hildesheim A, Gonzalez P, Pinto LA; Costa Rica HPV Vaccine Trial (CVT) Group. J Natl Cancer Inst. 2020 Oct 1;112(10):1038-1046. doi: 10.1093/jnci/djaa011. PMID: 32091594; PMCID: PMC7566548.

The CVT was a blinded, randomized, phase III clinical trial conducted as a collaboration between investigators in Costa Rica and the National Cancer Institute.

The investigators studied the durability of vaccine efficacy (VE) against human papillomavirus (HPV)16 or 18 infections and antibody response among non randomly assigned women aged 18 to 25 years, who received a single dose of the bivalent HPV vaccine and compared it with women who received multiple doses and also unvaccinated women.

HPV Vaccine: Cervarix, a bivalent HPV-16/18 virus-like particle (VLP) vaccine developed

by NCI and other research institutions and manufactured by Glaxo Smith Kline Biologicals.

The enrollment began in June 2004 and was completed in December 2005. A total of 7,466 participants were recruited. Eligible participants who consented were randomized to receive three doses of the HPV 16/18 (VLP) or a control Hepatitis A (Havrix) vaccine over a period of six months. Enrolled women were followed up for a period of four years and were screened for cervical neoplasia. At the end of initial four year trial participants were offered switch over vaccination. The original HPV arm was invited for participation in the long term follow-up. This follow-up involved biennial visits with pelvic examination and collection of cervical and blood samples for screening and antibody titres respectively, at each visit. A fresh characteristic matched unvaccinated control group (UGC) was included to substitute the control arm.

The 11 year follow-up of the Costa Rica HPV Vaccine Trial completed in August 2017. The HPV infections were compared amongst the various groups including those who received single dose (N=112), two doses (N=62), or three doses (N=1365), and age- and geographically-matched unvaccinated women (N=1783). Approximately 9 and 11 years (at two study visits) after initial HPV vaccination, the cervical HPV infections were measured using NCI next-generation sequencing TypeSeq1 assay. Vaccine Efficacy and 95% confidence intervals (CIs) were estimated. Antibody levels of HPV16 or 18 were measured in all one and two-dose women, and a randomly selected subset of three dose women, using a virus-like particle-based ELISA (n= 448).

Results: Median follow-up for the HPV-vaccinated group was 11.3 years (interquartile range =10.9–11.7 years). Vaccine Efficacy was 80.2% (95% CI ¼ 70.7% to 87.0%) ; 83.8% (95% CI ¼ 19.5% to 99.2%) and 82.1% (95% CI ¼ 40.2% to 97.0%) respectively among three, two and single dose recipient. There was no qualitative decline of HPV 16 or 18 antibody levels between 4 and 11 years regardless of the number of doses given, however antibody titers in one-dose group continued to be statistically significantly lower. The authors concluded that more than a decade after HPV vaccination, single-dose VE against HPV 16 or 18 infection remained high and HPV 16 or 18 antibodies remained stable. **A single dose of bivalent HPV vaccine may induce sufficiently durable protection that obviates the need for more doses.**

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021 May;71(3):209-249. doi: 10.3322/caac.21660. Epub 2021 Feb 4. PMID: 33538338.
2. https://hpvcentre.net/statistics/reports/IND_FS.pdf
3. https://www.who.int/news/item/11-04-2022-one-dose-human-papillomavirus-(hpv)-vaccine-offers-solid-protection-against-cervical-cancer

HPV Vaccine - The Journey and the Roadmap

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Introduction

Cervical cancer is the most common HPV-associated cancer worldwide, with the majority of cases and deaths occurring in lower-income countries. In India, it is the second most common cancer in women after carcinoma breast in India, with an estimated 123,907 new cases and 77,348 deaths annually, which is approximately 20% of the global burden.[1] Persistent infection with oncogenic types of human papillomavirus (HPV) has been shown to be the necessary cause of cervical cancer.[2]

To date, more than 100 HPV types have been identified. Depending on the oncogenic potential, various mucosal HPV types are categorized as either high-risk HPV/oncogenic HPV types or low-risk HPV/non-oncogenic HPV types. Approximately 15 HPV types are classified as high risk (16,18,31,33,35,39,45,51,52,56,58,59 ,68,73&82). High-risk HPV types 16/18 account for ~70% of cervical cancer globally and ~82.7% cancers in India. About 75% of sexually active individuals harbour at least one HPV type during their lifetime.

Cervical cancer is a preventable cancer as it has a long precancerous phase and with availability of screening methods for early detection and highly efficacious treatment. HPV tests have been developed for screening and prophylactic HPV vaccines have been developed against the major types. HPV vaccination is the optimal strategy for primary prevention of infection by some types of HPV that cause cervical cancer. Risk of HPV infection can be reduced by an HPV type-specific targeted vaccine, which produces a robust immune response, as compared to the natural infection which induces a very weak response and may not lead to protection against reinfection. According to the results of a comparative modelling analysis by Brisson et al, high HPV coverage and screening both are necessary to achieve elimination across all low-middle income countries (LMICs). Thus, introduction of vaccination along with screening is the pragmatic way to prevent cervical cancer.

History of HPV Vaccine Development

After identification of HPV as the primary cause of cervical cancer in the 1980s, studies conducted on animal models demonstrated that protection against papillomavirus lesions is possible using purified virions, and neutralizing antibody was necessary and sufficient for protection against viral challenge, and that protection was likely specific to HPV type. HPV vaccines are based on virus-like particles (VLPs) that are formed by HPV surface components. VLPs are not infectious because they lack viral DNA. However, they closely resemble the natural virus, and antibodies against VLPs have activity against the natural virus. The VLPs have been found to be strongly immunogenic, which means that they induce high levels of antibody production by the body. This makes the vaccines highly effective.

Types of Vaccine

Since the first HPV vaccine was licensed in 2006, there have been changes in regulatory indications and vaccination policy. Both the bivalent and quadrivalent vaccine were first licensed by FDA for prevention of HPV infection for girls and women aged 9 to 26 years. HPV vaccines have been licensed in India since 2009 for females aged 9 to 45 years. In 2018 the nonavalent vaccine was approved by FDA extending the age of vaccination upto 45 years. In India, these three prophylactic vaccines are available: bivalent vaccine Cervarix® (Glaxo Smith Kline), quadrivalent vaccine Gardasil® (Merck) and nonavalent vaccine Gardasil-9® (Merck). Recently a bivalent HPV vaccine Cecolin (Xiamen Innovax Biotech Co. Ltd) has been licensed in China and has received WHO prequalification in 2021, but is not available globally. All four vaccines prevent infections with high-risk HPV types 16 and 18. Gardasil-9 prevents infection with five additional high-risk HPV types (31, 33, 45, 52, and 58). In addition,

Gardasil® and Gardasil-9 prevents infection with non-oncogenic HPV types 6 and 11, which cause 90% of genital warts.[6] All these vaccines contain VLPs of the L1 protein produced in cultured cells and are formulated with adjuvants to increase their immunogenicity.

In a promising step in the fight against cervical cancer, India recently launched its first locally produced HPV vaccine, Cervavac, on 1st September 2022. The quadrivalent vaccine, which protects against HPV 16,18,6,11 strains, most likely to cause cancer of the cervix, vagina, vulva. It is jointly developed by the Serum Institute of India (SII) and the Indian Government's Department of Biotechnology (DBT). Following positive data from a large phase 2/3 clinical trial, marketing authorisation was granted by the Drugs Controller General of India (DCGI) on July 12, 2022, for girls and boys aged 9–26 years. The vaccine is more affordable than existing counterparts and will be soon available for commercial use. This could help in bridging the gap between screening and prevention both in India and other low-income and middle-income countries.

Table 1. shows the comparison of the HPV vaccines available in India.

Table 1: Comparison of HPV vaccines available for use in India

	Cervarix®	Gardasil®	Gardasil-9®	Cervavac
Manufacturer	Glaxo Smith Kline	Merck & Co. Inc	Merck & Co. Inc	Serum Institute of India Ltd.
HPV types	16,18	6,11,16,18	6,11,16,18,31,33,45,52,58	6,11,16,18
Substrate	Trichoplusia ni (Hi 5) insect cell line infected with L1 recombinant baculovirus	Saccharomyces cerevisiae expressing L1 (yeast)	Saccharomyces cerevisiae expressing L1 (yeast)	Recombinent Hansenula polymorpha (yeast)
Adjuvant	Aluminium hydroxide (AS04), 3-deacylated monophosphoryl lipid A	Aluminium hydroxyphosphate sulfate	Aluminium hydroxyphosphate sulfate (AAHS)	Aluminium hydroxide
Injection schedule	0,1,6 months	0,2,6 months	0,2,6 months	0,2,6 months

HPV vaccine schedules and introduction:

The uptake of HPV vaccines since their introduction has been highly variable and broadly correlated with country income levels. The HPV vaccination programs were initially predominated by high-income countries (HIC) and introduction in low-income countries (LIC) was largely dependent on external support that too through limited-scale demonstration projects. In 2012, Gavi initiated support for HPV vaccination to encourage its introduction in LIC.

CDC's Advisory Committee on immunization Practices (ACIP) and the American College of Obstetricians and Gynaecologists (ACOG)[3,4] recommends routine HPV (bHPV or qHPV) vaccination for girls and boys aged 11-12 years. ACIP also recommends a catch-up vaccination for all through ages 26 years if not adequately vaccinated previously.

FOGSI GCPR also recommends vaccination in 9-14 years old girls. Catch up vaccination in 15-26 year should be considered only if resources are available and with an understanding that vaccination in sexually active females may be less effective, but may provide some benefit against the types not exposed before.[5] Indian Academy of Paediatrics Committee on immunisation (IAPCOI) recommends that all females should receive HPV vaccine, if affordable, starting from 9 years of age and catch up vaccination at age 13 through 45 years, if not already vaccinated.[6]

WHO recommends 9 to 14 years aged females as primary target age group for vaccination and vaccination of older females only if it is affordable and cost effective and does not divert resources from vaccinating the primary target population or screening for cervical cancer. The current policy advises two doses of the vaccine for 9- to 14-year-old girls, while girls 15 and older as well as the immunocompromised, beginning at age 9, should receive three doses. WHO guidelines allow for flexibility in the timing of the second dose of the two- dose schedule, as early as five months after the first dose and with no

maximum recommended interval (though up to 12 to 15 months is suggested). According to the recommendations, persons aged 15 years or older, or those who are immunocompromised, including those who are HIV infected, should continue to receive three doses as per original dosage recommendations.

In April 2022 convening SAGE recommended updating dose schedules for HPV and WHO paper published in June 2022 endorse the same. The recommendations are 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 women, including those with living with HIV, should receive three doses if feasible, and if not, then at least two doses. There is limited evidence regarding the efficacy of a single dose in this group. However the WHO position paper and guidelines regarding single dose recommendations are awaited.

Barriers to HPV vaccination

Several factors have resulted in slower introduction of HPV vaccines in LMICs. Lack of awareness about cervical cancer and the role of HPV vaccine in its prevention, and concerns about their safety have been the major barriers. The cost of the vaccines, delay in provision of financial mechanisms to support countries in obtaining the vaccine and vaccine supply also pose a challenge. The supply currently available to LMICs is insufficient to meet the demand, leaving them unable to scale-up with the HPV vaccination programs as per WHO recommendations. The most prominent factor affecting current HPV vaccines for public health worldwide is their high cost. The vaccines offered in developing countries are still expensive to afford even at half price. In India, HPV vaccines have not yet been introduced by the government in the National Immunization Program. The sustained financial commitment for the cost of vaccine procurement and vaccine delivery in LMICs has been a key factor for hesitancy to introduce HPV vaccine in national immunisation program. Thus, various approaches have been suggested to make the HPV vaccine more affordable for LMICs, including integrating vaccination into existing adolescent or school-health programs. A single-dose regimen for HPV vaccines could be another way to reduce costs and simplify delivery. However, integration has proved challenging in many settings since these programs operate only in selected districts of a country or are not functioning effectively. A dose-reduction recommendation to a single-dose regimen will potentially reduce the costs of vaccine supply and delivery since different delivery strategies might be available for a single-dose schedule.

FAQs related to HPV vaccination

Is the vaccine safe?

Safety and efficacy of HPV vaccine has been established by a large number of trials conducted with thousands of girls and young women as well as post-marketing surveillance with no serious adverse event linked to the HPV vaccine. WHO global advisory committee for vaccine safety (GACVS) regularly reviews evidence related to safety of HPV vaccine.

Are there any contraindications or side effects of the vaccine?

Severe allergic reaction to any vaccine component or following a prior dose of HPV vaccine is a contraindication for vaccination. The most commonly observed side effects are mild and include injection site pain and redness, occasionally a mild fever.

How long does vaccine protection last?

Continued protection and persistent antibody levels have been observed through a minimum of 10 years following vaccination among female participants against high-grade cervical, vaginal and vulvar neoplasia. There has been no evidence to suggest that the HPV vaccine loses ability to provide protection over time.

Can HPV vaccination be done in older age group women?

HPV incidence decreases with age, women more than 25 years remain at risk of developing new HPV infections. For women aged 25 to 45 years,

the first priority should be given to cervical cancer screening and prior to vaccinating these women counselling should be done about reduced efficacy of vaccine.

Is Vaccine effective in sexually active females?

The effectiveness of vaccine will depend on past exposure to the virus. HPV vaccines targets the most common hrHPV types. The protection they provide is strongest for the HPV types in the vaccine that a person has not yet been exposed to. In general, people contract one or more these types of the virus soon after becoming sexually active. So to benefit fully from the vaccine, it is best to be vaccinated before initiating sexual activity.

Will it be better to wait and vaccinate girls when they are older?

No. There is no reason to wait until girls are older than the recommended 9–14 years of age to get the vaccine. The HPV vaccine produces a stronger immune response at this age than later in life and it is most effective if given before a person comes in contact with the targeted HPV types. HPV is most prevalent among women younger than 25 years of age, so many become infected within just a few years of starting sexual activity. This is true even for women who have only one sexual partner.

Is HPV vaccine safe during pregnancy and lactation?

HPV vaccination is not recommended during pregnancy, but if a woman becomes pregnant after starting the vaccination schedule, termination is not required. Further vaccination should be withheld and remaining dose(s) given post-delivery without repeating the initial dose(s). Lactation is not a contraindication for HPV vaccination.

Will HPV vaccine influence sexual behaviour or choices of girls?

There is no evidence that the vaccine will impact future sexual behaviour of vaccinated girls. Giving a child the HPV vaccine reduces or eliminates the risk of cervical and other cancers, cervical lesions, and genital warts and is a positive step to improve child's future health and wellbeing.

Will HPV vaccine affect fertility?

HPV vaccination does not affect a girl or woman's chance of getting pregnant or in any way impact future pregnancies. It also does not affect the fertility of boys or men. It is an important step in preventing the long-term consequences of HPV infection, which can include cervical cancer, infertility or even death.

Should boys be vaccinated?

Both the nonavalent and the indigenous Cervavac have been licensed for use in boys as well, and they will benefit by protection against anal, penile and oropharyngeal cancers as well as genital warts. However, given the global shortage of HPV vaccines, WHO recommends that vaccination of girls should be the first target. Modeling studies also show this to be a more effective strategy.

Should older women be vaccinated?

The main benefit of vaccination comes when it is given before sexual debut. However, there is no adverse effect in giving to older women, so long as they are able to afford it and are aware about the need for screening, preferably by HPV testing.

Roadmap for the future

In May 2018, the WHO Director-General announced a global call for action to eliminate cervical cancer, underscoring renewed political will to make elimination a reality and calling for all stakeholders to unite behind this common goal. Following the call from the WHO, in 2020, the World Health Assembly passed a resolution calling for elimination of cervical cancer and adopting a global strategy which was officially launched on 17th November 2020.

The WHO global strategy outlines the following threshold: to eliminate cervical cancer as a public health problem globally, all countries must work towards an incidence rate of less than 4 cases per 100,000 women-years.[3] Achieving that goal rests on three key pillars and their corresponding targets:

- Vaccination: 90% of girls fully vaccinated with the HPV vaccine by the age of 15 years
- Screening: 70% of women screened using a high-performance test by the age of 35, and again by the age of 45 years
- Treatment: 90% of women identified to have cervical pre-cancer and invasive cancer adequately treated.

Each country should meet the 90-70-90 targets by 2030 to get on the path to eliminate cervical cancer within the next century.

There has been tremendous effort globally for primary and secondary prevention of cervical cancer. In India, progress has been made in term of the development of new indigenous HPV vaccine which was launched recently and soon it will be rolled out for commercial use in phases. It is recommended for use as two dose in <15 years girls and boys and as three doses for those ≥15 years. For single dose recommendations for this vaccine more studies are required to observe sustained immune response of the vaccine. WHO has endorsed the recommendations for single dose vaccination with available HPV vaccines (Cervarix, Gardasil and Gardasil9) and the guideline for implementation of single dose schedule is awaited.

Conclusion

Incorporation of HPV vaccination in national immunization programme for prevention of cervical cancer is the need of the hour. Gynaecologists play a crucial role in imparting knowledge and creating awareness among the eligible women and girls for vaccination and screening. However, vaccination will help in reducing the risk of cervical cancer in the future and screening programmes are an equally important intervention for prevention and early detection of cervical cancer to advance the pace of elimination. Though all the vaccines are equally good, nonavalent vaccine provides wider coverage than the quadrivalent vaccine. On long-term follow-up, even after single-dose HPV vaccination, the antibody titer remains good. Herd immunity can also be achieved by HPV vaccination. Hence, mass single-dose nonavalent HPV vaccination for sexually naive preadolescent girls can provide almost 100% protections and a cost-effective approach for the developing countries.

Suggested Reading:

1. Sung H, Ferlay J, Seigel R, Laversanne M, Soerjomataram I, Jemal A et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin 2021;71:209–49
2. RodriguezA.C, SchiffmanM, HerreroR, et al. Longitudinal study of human papillomavirus persistence and cervical intraepithelial neoplasia grade 2/3: critical role of duration of infection. J Natl Cancer Inst. 2010;102(5):315-24.
3. Committee opinion no. 641: Human Papillomavirus Vaccination. Obstet Gynecol 2015;126:e38–43.
4. Saslow D, Andrews K S, Manassaram-Baptiste D, Smith R A, Fontham E T.H. Human papillomavirus vaccination 2020 guideline update: American Cancer Society guideline adaptation. CA Cancer J Clin 2020;70(4):274-80.
5. FOGSI GCPR on Screening and Treatment of Preinvasive lesions of the cervix and HPV vaccination. Available from URL https://www.fogsi. org/fogsi-gcpr-on-screening-management-of-cervical-precan cerous-lesions/
6. Indian Academy of Pediatrics (IAP) Recommended immunization schedule for Children aged 0 through 18 years – India, 2014 and Updates on immunization Indian Pediatrics 2014; 51: 785-800.
7. WHO. 2022. One-dose Human Papillomavirus (HPV) vaccine offers solid protection against cervical cancer. Accessed 14.10.2022. https://www.who.int/news/item/11-04-2022-one-dose-human-papillomavirus-(hpv)-vaccine-offers-solid-protection-against-cervical-cancer.

Preventing Cervical Cancer -Global Strategies

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Cervical cancer is preventable and curable if detected early and adequately treated. Despite this fact, Cervical cancer is the fourth most common cancer among women globally. The annual number of new cases of cervical cancer has been projected to increase from 5,70,000 to 7,00,000 between 2018 and 2030, with the annual number of deaths projected to increase from 3,11,000 to 4,00,000. It is a disease of inequality, with the incidence in low and middle-income countries nearly twice as high and its death rate nearly three times as high as in high-income countries.

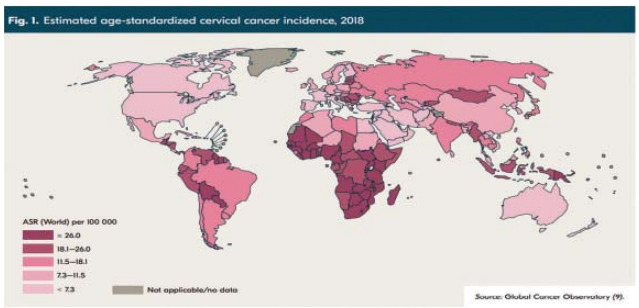
Why is the Global strategy needed?

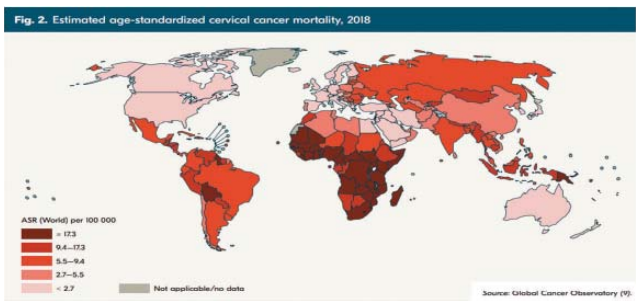
All countries are affected with cervical cancer and the age-standardized incidence rates vary from 75 per 1,00,000 women in the highest-risk countries to fewer than 10 per 1,00,000 women in the lowest-risk countries.[1] (Fig 1) So, Global Strategies are urgently needed to optimally implement measures at national level to eliminate cervical cancer. The suggested provisions are :

- The vision of a world where cervical cancer is eliminated as a public health problem;
- A threshold of 4 per 1,00,000 women-years for elimination as a public health problem;
- To follow 90-70-90 targets that must be met by 2030 for countries to be on the path towards cervical cancer elimination. It proposes that 90% of girls are fully vaccinated with HPV vaccine by the age of 15 years, 70% of women are screened with a high-performance test by 35 years of age and again by 45 years of age. And 90% of women identified with the cervical disease receive treatment (90% of women with precancer, and 90% of women with invasive cancer are managed effectively).

The implementation of this vision needs political will and is to be delivered using health service platforms.

This is the first global health strategy for the elimination of cervical cancer as a public health problem. It is influenced by by the Director-General's call in May 2018 to all countries to take action to help end the suffering caused by cervical cancer. In this he spoke for renewed political will to realize elimination and urged all stakeholders to unite behind this common goal.[2] Nearly 90% of the 3,11,000 deaths worldwide in 2018 occurred in low and middle-income countries (Fig. 2).





HPV and Cervical Cancer

The primary cause of precancerous and cancerous cervical lesions is infection with a high-risk or oncogenic human papilloma virus (HPV). HPV makes up a group of viruses that are extremely common worldwide. There are more than 100 types, of which at least 14 cause cancer. HPV 16 and 18, are responsible for about 70% of cervical cancer worldwide. Infection with certain HPV types also causes a proportion of cancers of the anus, vulva, vagina, penis and oropharynx, which are preventable using primary prevention strategies similar to those for cervical cancer.[3]

HIV and Cervical Cancer

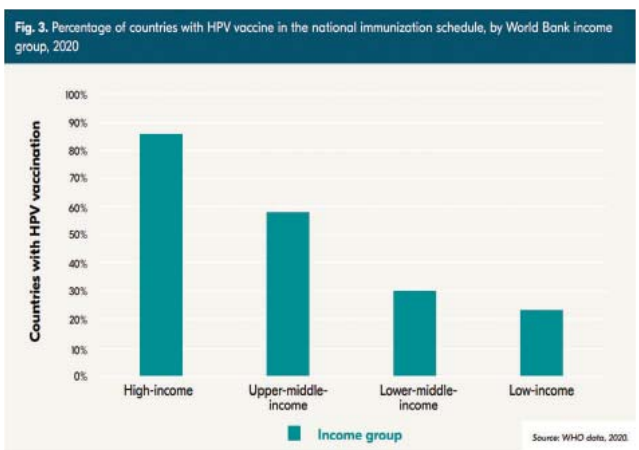
Cervical cancer is the most common cancer

among women living with HIV. Women living with HIV are six times more likely to develop cervical cancer. [4] Despite the gains in prolonged life expectancy associated with access to HIV care and treatment in countries worst hit by the HIV epidemic, cervical cancer in women living with HIV has not received the attention and resources that are needed to address its prevention and treatment, and screening coverage has often been low. Reaching vulnerable women at high risk of developing cervical cancer and acquiring HIV infection needs prioritization of integrated preventive, screening, and treatment services to maximize the impact.

Cervical Cancer Control Interventions: Current Status of Access to HPV Vaccines, Screening and Treatment

Between 2006 and 2017, more than 100 million adolescent girls worldwide received at least one dose of the HPV vaccine, 95% of whom were in high-income countries. As of 2020, less than 25% in low-income and less than 30% in lower-middle-income countries had introduced.

the HPV vaccine into their national immunization schedules, while more than 85% of high-income countries had done so (Fig. 3). A similar breakdown is observed in the establishment of cervical cancer screening programmes and availability of cancer management services when examining countries based on income level.[5]



Around 30% of low-income countries reported having pathology services, cancer surgery, chemotherapy, and radiotherapy units generally available in the public sector, compared with more than 90% in high-income countries.

The Path to Elimination of Cervical Cancer

The huge burden of mortality related to cervical cancer is a consequence of decades of neglect by the global health community. Clearing the path to cervical cancer elimination will require bold strategic actions.

Principles and Goals

To eliminate cervical cancer as a public health problem globally, all countries must work towards an incidence below 4 per 1,00,000 women-years. The elimination threshold is achievable in the vast majority of countries, including the 78 low and lower-middle-income countries with the highest burdens of disease.[6] Implementing all the three pillars of the strategy will contribute to the immediate and accelerated reduction in mortality rates. Incidence rates will gradually decrease as a result of wide-scale implementation of the population-based screen and treat services, and vaccination against HPV.

Impact of Achieving the 2030 Targets on Incidence and Mortality in High-Burden Countries

The WHO Secretariat modelled the health and socioeconomic impacts of achieving the 90-70-90 targets by 2030 in 78 low and lower-middle-income countries. The current heterogeneity in incidence between countries will lead to ongoing variations in cervical cancer incidence and the time frame to reach elimination. Figure 4

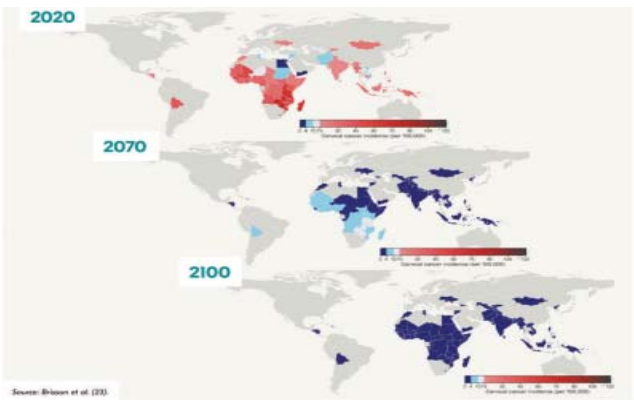


Figure 4-Age-standardized cervical cancer incidence rate in 78 low- and lower-middle-income countries in 2020, 2070 and 2100 after implementation of the elimination strategy

Strategic Actions to achieve the 2030 targets

Strategic actions to achieve the 90-70-90 targets should be pursued within the framework of a national policy to eliminate cervical cancer. WHO recommends a **life-Course Approach** to a comprehensive strategy for cervical cancer elimination to ensure that lifetime benefits are maintained.

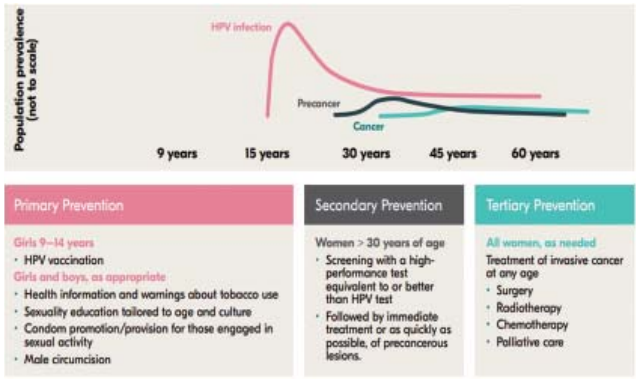


Figure 5 – Life Course Approach

Primary Prevention: HPV Vaccination

Vaccination of adolescent girls is the most effective long-term intervention for reducing the risk of developing cervical cancer. The great long-term benefit of HPV vaccination makes it important to initiate and sustain this approach in all countries. There is also strong evidence that high HPV vaccination coverage leads to the protection of unvaccinated individuals through herd immunity, further enhancing the protective effect on the community.[8] WHO's current guidelines recommend that young adolescent girls between 9 and 14 years receive two doses of vaccine to be fully protected. Data suggesting protection after a single dose have led to trials that will provide evidence for future schedule optimization.[9,10] To ensure high levels of acceptance and sustained coverage, the introduction of HPV vaccination programmes must be accompanied by strong communication strategies for advocacy and social mobilization to affirm the efficacy, safety and benefits of the vaccine. In addition to HPV vaccination, a comprehensive prevention strategy must include age-appropriate information on sexual and reproductive health, safer sexual practices – such as delaying sexual debut, decreasing the number of sexual partners, condom use, and male circumcision.

where appropriate and cessation of tobacco. Concerted efforts to promote healthy lifestyles among adolescents (boys and girls) are critical for a healthier population for sustainable development.

Strategic Actions to achieve 90% coverage of HPV Vaccination

1. Secure sufficient and affordable HPV vaccines
2. Increase the quality and coverage of vaccination by involving efficient and sustainable multisectoral delivery platforms (such as school immunization programmes) and innovative community-based approaches to reach vulnerable populations (such as adolescent girls who are not in school). Monitoring systems or registers should track and improve coverage and quality.
3. Improved nationwide, evidence-based communication and social mobilization efforts which will require an understanding of social, cultural, societal and other barriers that may affect the acceptance and uptake of the vaccine.
4 National guidelines, policies, and strategies to improve the efficiency of vaccine delivery should be updated as new evidence and innovations become available.

Secondary Prevention: Screening and Treating Precancerous Lesions

The principal goal of secondary prevention is to reduce cervical cancer incidence and mortality by identifying and treating women with precancerous lesions. Cytology-based screening has been successfully used to achieve these goals when implemented as part of national programmes with high coverage and in settings where resources exist for patient follow-up, additional diagnostic tests (colposcopy and pathology) and disease management.

In low- and middle-income countries cytology-based programmes have been difficult to implement, and where they have been implemented, the screening coverage is low. Visual inspection of the cervix with acetic acid followed by treatment (screen and treat) is an alternative approach to secondary prevention

in resource-constrained settings. Although relatively easy to establish, the quality of such procedure is influenced by the quality of service provider and its sensitivity is variable.

Testing for HPV offers superior specificity. Its strong negative predictive value suggests that women who test negative, need to be retested after five years. Providing women with the option of self-sampling contributes to acceptability and access to services. Existing technological platforms being used in countries to test for HIV, tuberculosis and other infections can also be used for HPV testing, enabling rapid scale-up. Because of its high level of performance, countries should ideally promote transition to HPV testing as the primary method of screening for cervical cancer. Evidence-based strategies for the evaluation and management of women who test HPV-positive are available.

Cervical cancer screening will require a matching increase in capacity for treatment of the detected lesions, as screening women without access to treatment is unethical. WHO's treatment guidelines were recently expanded to include thermal ablation as a therapeutic modality for women who have precancerous lesions eligible for ablation.[11] Market-shaping initiatives to secure affordable, high-quality diagnostics and related supplies should be prioritized. Research on artificial intelligence-based diagnostic technology and simple handheld devices for ablative therapy offers immense opportunities and moves the world closer to the vision of cervical cancer elimination.[12]

Strategic Actions to Achieve 70% Coverage for Screening and 90% Treatment of Precancerous Lesions

1. Understand barriers to access services and create an enabling environment. A robust understanding of the social, cultural, societal and structural barriers to the uptake of services is crucial. Such knowledge will help to design acceptable, accessible service delivery platforms. Local communities, especially women, must be engaged and empowered. Increasing health literacy, knowledge of rights and awareness of cervical cancer prevention and control will help to mobilize, empower and engage communities and civil society.
2. Integrate screening and treatment services into the primary care package - Services integrated into existing sexual and reproductive health services, HIV care and treatment clinics, antenatal care, well-women clinics and school-based health outreach are points of entry for reaching women and girls.
3. Promote a screen and treat approach- Countries will need to expand the number of facilities where a single-visit screen and treat approach could be implemented.
4. Ensure an affordable supply of quality-assured, high-performance screening tests and treatment devices- Prompt registration and market shaping for cervical cancer diagnostics and treatment devices will lead to improved access and affordability. WHO will strengthen its prequalification capacity, as appropriate, to remain abreast of emerging technologies.
5. Strengthen laboratory capacity and quality assurance programmes- Efficient, integrated networks of laboratory services will maximize the impact of limited human and financial resources. Training and supervision must be an integral component of service delivery.

Invasive cancer treatment and palliative care

Timely assessment and referral of women with suspected or confirmed cervical cancer are crucial for saving lives. Comprehensive management of invasive cervical cancer requires well-equipped, appropriately qualified health providers and access to pathology, medical imaging, surgical, radiotherapy and chemotherapy services. The five-year survival rate for early-stage cancer is more than 80% in countries where timely diagnosis and high-quality treatment are available. Surgery and radiotherapy, with or without chemotherapy, are among the cost-effective interventions that WHO recommends for early-stage cervical cancer.[13] Even some locally advanced cervical cancers are curable with high-quality concurrent chemoradiation.[14] Palliative care should be integrated into the treatment plan and provided throughout the course of the disease.[15] Common treatment-related effects experienced by long-term

cervical cancer survivors that affect the quality of life include bladder dysfunction, bowel dysfunction, sexual dysfunction, lymphoedema and psychosocial problems. Currently, very few low and middle-income countries have palliative care programmes in place. Countries are encouraged to expand the availability of palliative care services, which could readily be extended to other forms of advanced cancers and to a non-malignant debilitating disease. In addition to managing pain and other distressing symptoms, care should encompass psychosocial and spiritual support for women and their families.[16]

Strategic Actions to Achieve 90% Treatment and Care for Cervical Cancer Cases

1. Implement cervical cancer management guidelines - Developing and implementing national cervical cancer management guidelines is central to ensuring high-quality care.[17]
2. Establish referral pathways and people-centred linkages - Streamlining care pathways and referral networks linking all levels of care will ensure the timely management of patients.
3. Strengthen pathology services - Access to high-quality pathology services is crucial for the management of invasive cancer. The development of regional pathology centres, making use of affordable telepathology platforms, is possible for countries with limited or no capacity to interpret samples.[18]
4. Expand surgical capacity -The cancer patients who live in the world's poorest countries, less than 5% have access to safe, effective and timely cancer surgery.[19] In high-income countries the predominant model of postgraduate surgical oncology education consists of multiyear speciality training within accredited programmes, supported by experienced board-certified oncological surgeons and a sophisticated, highly functional surgical infrastructure. In most low- and middle-income countries the health care providers performing oncological procedures are general surgeons & gynaecologists, general practitioners without formal, certified subspecialty training, who provide cancer care out of necessity. Novel attempts to scale up surgical capacity in these environments using focused, competency-based training and North-South twinning partnerships have met with success and should be expanded.[20]
5. Improve access to radiotherapy and chemotherapy. Most patients with cervical cancers in low- and middle-income countries present at stages that require radiation, so sustainable capacity for curative radiation therapy is critical.
6. Strengthen and integrate palliative care services. Treatment plans should incorporate not only end-of-life care and pain relief for patients but also psychological support, family support and other services from the outset. Home-based models of palliative care should be integrated into primary health care.
7. Optimize health workforce competencies throughout the continuum of care - A strategy for long-term national health workforce education and training, recruitment and retention is the key to ensuring sustainable multidisciplinary team-based care. The WHO Global Strategy on Human Resources for Health: Workforce 2030 provides a blueprint for countries to address workforce challenges.[21]
8. Reduce cancer stigmatisation by patient awareness, especially through survivor groups.
9. Provide comprehensive support designed to enhance the quality of life and address physical, psychological, social and spiritual challenges faced by survivors. Such programmes are best developed locally, tailored to the sociocultural context.

Health System Enablers

Strengthening health system enablers. There is a renewed commitment to primary health care as the pathway for all countries working towards universal health coverage. Primary care should remain the preferred entry point for cervical cancer prevention interventions but service structures need to accommodate women presenting at any point in the system. Such efforts should be mutually reinforcing

and facilitate the integration of cervical cancer services with other specific programmes.

Priority actions to strengthen health systems

1. Reinforce primary healthcare-oriented models of care in the country's programmes that promote high-quality, people-centred primary health care throughout the life course.
2. Invest in the primary health care workforce - A sufficiently sized health workforce, with staff who have an optimal mix of skills and who are competent and equitably distributed, can support the delivery of new cervical cancer prevention and treatment interventions, as well as palliative care services.
3. Availability and affordability of appropriate, safe, effective, quality medicines and other health products are central to the elimination targets.
4. Reduce cancer stigmatisation.
5. Engage with private sector providers for the delivery of integrated health services is required to ensure depth of coverage and affordable access to all.
6. Universal health coverage and protection from catastrophic costs - Cervical cancer programmes must be fully integrated into universal health coverage. Sustainable financing should be secured through domestic resource mobilization, increased efficiencies in the health system, and ensuring that user fees are not imposed on the poorest. Health financing and protection systems, and care delivered closer to where women live and work, are core to achieving elimination.
7. Innovation and digital technologies can facilitate access to cervical cancer services, improve effectiveness and efficiency, and promote accountability.
8. Systems for improving the quality of health care at the local, subnational and national levels for continuously assessing and improving the quality of integrated health services are important.
9. Data systems, monitoring and evaluation through well-functioning health information systems that generate reliable data on progress towards cervical cancer elimination can support improved decision-making and learning by local, national and global actors.

Partnerships, Advocacy and Communication

Partnerships with global institutions, development partners, and multilateral and bilateral entities will play a crucial role, particularly in resource mobilization and strategic policy dialogue. Ongoing work with other organizations in the United Nations system will be strengthened. Partnerships with professional associations and academic institutions will also contribute to capacity building, skills transfer and strengthening existing collaboration. The role of local networks is fundamental to the successful uptake of services at the community level. Innovative ways must be found to secure sustainable resources for these partnerships. Collaborations must allow multiple sectors to agree on and pursue a common vision through maximizing comparative advantages. The Global Action Plan for Healthy Lives and Well-being for All provides a sound platform to support country-led implementation of strategies to achieve Sustainable Development Goal 3 and the targets of other health-related Goals.[22]

Effective advocacy and communication strategies should involve media platforms, opinion leaders, influencers, traditional and faith leaders, and patient advocates should be deployed strategically in order to increase access to information. The WHO guidance on community mobilization, education and counselling for cervical cancer prevention and treatment can be used to improve health literacy.[23]

Surveillance, Monitoring and Evaluation

The scale-up of cervical cancer prevention activities cannot proceed without the framework and tools to assess and evaluate progress towards cervical cancer elimination. It is fundamental that robust surveillance and monitoring systems are developed at the national or subnational level.

Monitoring and evaluation also enable programme managers to identify gaps and take specific actions to improve coverage, quality and outcomes. Fig.6 illustrates a framework for data collection and indicator development and the different strategies required to obtain such information, differentiating two major components: population-based surveillance and programme monitoring.

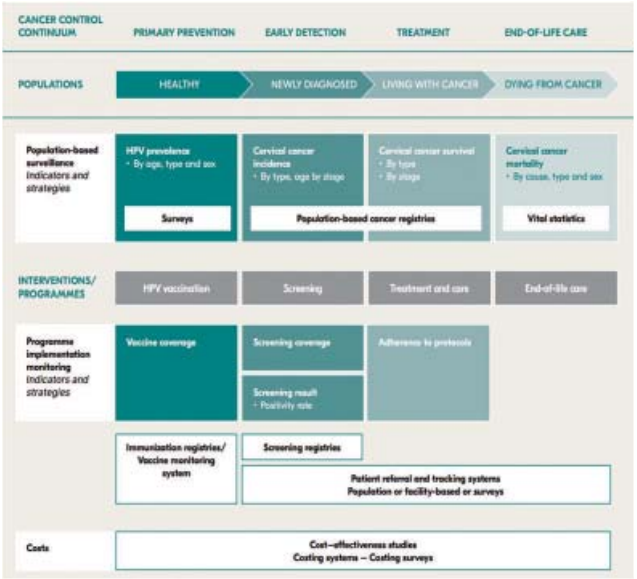


Figure 6

Accountability for Impact

The WHO Thirteenth General Programme of Work 2019–2023 provides the strategic vision for the work of WHO. The cross-organizational nature of the strategy will help ensure the provision of better-aligned support for implementation. The Impact Framework of the General Programme of Work will strengthen accountability for impact. Implementation will focus on strengthening existing programmes and collaborating more closely with partners and organizations in the United Nations system currently providing technical assistance for prevention, screening, and treatment and management of cervical cancer.

Implementation

All six WHO regions have strategies or plans for cervical cancer control that reflect the diverse nature of challenges and offer opportunities to scale up all three pillars of the prevention-to-care continuum. Each region has a range of strategic partnerships, agencies, and institutions with context-specific expertise to support implementation of the global strategy. To ensure alignment with the global strategy, the Secretariat will support Member States in implementation as outlined in the mandate from the World Health Assembly when it endorses the strategy.

References

1. Global Cancer Observatory. Estimated cancer incidence, mortality and prevalence worldwide in 2018: cervical cancer. International Agency for Research on Cancer, World Health Organization; 2018 (https://gco.iarc.fr/today/data/ factsheets/cancers/23-Cervix-uteri-fact-sheet.pdf, accessed 2 October 2020).
2. Cervical cancer: an NCD we can overcome. Speech by WHO Director-General, 18 May 2018. Geneva: World Health Organization; 2018 (https://www.who.int/dg/speeches/detail/cervical-cancer-an-ncd-we-can-overcome, accessed 2 October 2020).
3. de Martel C, Plummer M, Vignat J, Franceschi S. Worldwide burden of cancer attributable to HPV by site, country and HPV type. International Journal of Cancer. 2017;141(4):664–70. doi:10.1002/ijc.30716.
4. Abraham A, D'Souza G, Jing Y, Gange S, Sterling T, Silverberg M et al. Invasive cervical cancer risk among HIV infected women: a North American multicohort collaboration prospective study. Journal of Acquired Immune Deficiency Syndromes. 2013;62(4):405–13. doi:10.1097/QAI.0b013e31828177d
5. Assessing national capacity for the prevention and control of noncommunicable diseases: report of the 2019 global survey. Geneva: World Health Organization; 2020 (https://apps.who.int/iris/handle/10665/331452, accessed 2 October 2020).
6. Brisson M, Kim JJ, Canfell K, Drolet M, Gingras G, Burger EA, et al. Impact of HPV vaccination and cervical screening on cervical cancer elimination: a comparative modelling analysis in 78 low-income and lower-middle-income countries. Lancet. 2020;395(10224):575–590. doi.org/10.1016/S0140-6736(20)30068-4
7. Vorsters A, Arbyn M, Baay M, Bosch X, de Sanjose S, Hanley S et al. Overcoming barriers in HPV vaccination and screening programs. Papillomavirus Research. 2017;4:45–53.)
8. Drolet M, Bénard E, Pérez N, Brisson M, on behalf of the HPV Vaccination Impact Study Group. Population-level impact and herd effects following the introduction of human papillomavirus vaccination programmes: updated systematic review and meta-analysis. Lancet. 2019;394(10197):497–509. doi:10.1016/S0140-6736(19)30298-3
9. Brotherton JM, Budd A, Rompotis C, Bartlett N, Malloy NJ, Andersen RL et al. Is one dose of human papillomavirus vaccine as effective as three? A national cohort analysis. Papillomavirus Research. 2019;8:100177. doi:10.1016/j.pvr.2019.100177.
10. Stanley M, Dull P. HPV single-dose vaccination: impact potential, evidence base and further evaluation. Vaccine. 2018;36(32 Pt A):4759–60. doi:10.1016/j.vaccine.2018.02.076

11. WHO guidelines for the use of thermal ablation for cervical pre-cancer lesions. Geneva: World Health Organization; 2019 (https://apps.who.int/iris/handle/10665/329299, accessed 5 October 2020).
12. Unitaid. Screening and treatment of pre-cancerous lesions for secondary prevention of cervical cancer: technology landscape. Geneva: World Health Organization; 2019 (https://unitaid.org/assets/Cervical_Cancer_Technologylandscape-2019.pdf, accessed 5 October
13. Cohen PA, Jhingran A, Oaknin A, Denny L. Cervical cancer. Lancet. 2019;393(10167):169–82. doi:10.1016/S0140- 6736(18)32470-X.
14. Eifel PJ, Winter K, Morris M, Levenback C, Grigsby PW, Cooper J et al. Pelvic irradiation with concurrent chemotherapy versus pelvic and para-aortic irradiation for high-risk cervical cancer: an update of radiation therapy oncology group trial (RTOG) 90-01. Journal of Clinical Oncology. 2004;22(5):872–80. doi:10.1200/JCO.2004.07.197.
15. Palliative care. In: Comprehensive cervical cancer control: a guide to essential practice, 2nd edition. Geneva: World Health Organization; 2014 (https://apps.who.int/iris/handle/10665/144785, accessed 5 October 2020).
16. Pfaendler KS, Wenzel L, Mechanic MB, Penner KR. Cervical cancer survivorship: long-term quality of life and social support. Clinical Therapeutics. 2015;37(1):39–48. doi:10.1016/j.clinthera.2014.11.013).
17. Chuang LT, Feldman S, Nakisige C, Temin S, Berek JS. Management and care of women with invasive cervical cancer: ASCO Resource-Stratified Clinical Practice Guideline. Journal of Clinical Oncology. 2016;34(27):3354–5. doi:3310.1200/JCO.2016.3368.3789
18. Montgomery ND, Tomoka T, Krysiak R, Powers E, Mulenga M, Kampani C et al. Practical successes in telepathology experiences in Africa. Clinics in Laboratory Medicine. 2018;38(1):141–50. doi:10.1016/j.cll.2017.10.011 .
19. Sullivan R, Alatise O, Anderson B, Audicio R, Autier P. Delivering safe and affordable cancer surgery to all. Lancet Oncology Commission on Global Cancer Surgery. Lancet Oncology. 2015;16(11):1193–224.
20. Chinula L, Hicks M, Chiudzu M, Tang J, Gopal S, Tomoka T et al. A tailored approach to building specialized surgical oncology capacity: early experiences and outcomes in Malawi. Gynecologic Oncology Reports. 2018;26:60–5.
21. Global Strategy on Human Resources for Health: Workforce 2030. Geneva: World Health Organization; 2016 (https://apps.who.int/iris/handle/10665/250368, accessed 5 October 2020)
22. Stronger collaboration, better health: global action plan for healthy lives and well-being for all: strengthening collaboration among multilateral organizations to accelerate country progress on the health-related Sustainable Development Goals. Geneva: World Health Organization; 2019 (https://apps.who.int/iris/handle/10665/327841, accessed 5 October 2020).
23. Community mobilization, education and counselling. In: Comprehensive cervical cancer control: a guide to essential practice, 2nd edition. Geneva: World Health Organization; 2014 (https://apps.who.int/iris/handle/10665/144785, accessed 5 October 2020).

Calendar of Virtual Monthly Clinical Meetings 2022-23

28th October, 2022	PGIMSR & ESI Hospital
12th & 13th November, 2022	**44th Annual AOGD Conference (Physical)**
25th November, 2022	VMMC & Safdarjung Hospital
30th December, 2022	Sir Ganga Ram Hospital
27th January, 2023	ABVIMS & Dr Ram Manohar Lohia Hospital
24th February, 2023	UCMS & Guru Teg Bahadur Hospital
31st March, 2023	MAMC & Lok Nayak Hospital
28th April, 2023	LHMC & Smt. Sucheta Kriplani Hospital
26th May, 2023	Sitaram Bhartia Hospital

Targeted Therapy-Beyond Chemotherapy Management Strategies in Cervical Cancer

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**Ex Senior Resident, Deptt of Pathology, UCMS & GTBH

Cervical cancer, although preventable, still remains second common cancer of females in India and is leading cause of deaths due to cancer. 15% of cervical cancer cases present as stage IV B and 5-year recurrence rates remain high (28–73.6% for stage IIB-IVB). Choices of treatment in such cases are few and patients are being treated with 2nd line systemic therapy with a mean overall survival time of around 7–9 months. There is an unmet need of novel therapies in persistent, recurrent or metastatic cancer. A recent insight into molecular biology of cancer cervix and success of target therapy in other solid tumours has invoked many research studies in cervical cancer.

Guidelines have included bevacizumab and Pembrolizumab in the systemic therapy for persistent, recurrent and metastatic cancer cervix. Both the drugs were given accelerated approval by FDA based on survival benefits proved by clinical trials. This review will include basics of target therapy, molecular targets of cancer cervix, clinical trials with modalities of target/ immunotherapy and recent protocols and guidelines.

Basics of Target therapy

Targeted therapy aims at delivering drugs to particular genes or proteins that are specific to cancer cells or the tissue environment that promotes cancer growth. Molecular targeted therapies are revolutionized therapeutics which interfere with specific molecules to block cancer growth, progression, and metastasis, promote cell cycle regulation or induce apoptosis or autophagy and targeted delivery of toxic substances specifically to cancer cells to destroy them. Its unlike chemotherapy which kills the rapidly growing cells and, in that process, also attacks the normal cells leading to toxic effects. Cancer therapy has evolved from blanket therapy to precision medicine which is specific, effective, and safe. Because of fewer side effects it maintains the quality of life.

Even though target therapy and immunotherapy are used interchangeably, they are not synonyms. **Target therapy aims to inhibit molecular pathways that are critical to tumour growth and maintenance, whereas immunotherapy endeavours to stimulate a host response that results in tumour destruction.**

Targetable molecules in cancer cervix (Table 1)

Box 1 A case of cancer cervix with relapse

Mrs X, 62years old, female was treated with chemoradiation for stage IIB cervical cancer & was disease free at end of therapy in July 2019.

Dec 2021 , on routine follow up she had solitary lung metastasis on PET CT with no evidence of disease anywhere else. Her ECOG performance status was 0.

1. What is next course of action.

1. What is next course of action.

   She underwent image guided pulmonary biopsy which revealed it as SCC. It was positive for PDL -1 receptors, CPS = 10.

   Prognosis in relapse cases with distant metastasis is poor. Patient was offered upper lobe lobectomy of right lung / focussed Radiotherapy with adjuvant chemotherapy. However, patient refused surgical intervention/RT and opted for systemic chemotherapy.

   Systemic CHT was given to her consisting of Day 1- Bevacizumab IV 15mg/kg, paclitaxel IV 175 mg/ m2 over 3 hrs followed by carboplatin AUC 5IV over 30 minutes, and pembrolizumab 200mg IV every 3 weeks for 6 cycles. Pembrolizumab was given for total of 10 cycles & discontinued because of cost of the drug. This may be continued for 35 cycles or till toxicity or progressive disease develops. At present her lung metastasis has disappeared and she is off all the drugs.

2. In cases of toxicity/ progressive disease second line single agents can be given as per NCCN guidelines. Promising target therapy will be tisotumab vedotin(TFTV). Target therapy maintains good quality of life.

Table 1 Target agents in treatment of persistent, recurrent and metastatic cancer cervix.

Agents	Targets
I Antiangiogenesis agents	
Bevacizumab (monoclonal antibody)	VEGEF EGFR
II Small molecule kinase inhibitors & monoclonal antibodies	
Erlotinib, Gefitinib and Cetuximab	
III Immunotherapy	
A) Immune checkpoint inhibitors (ICIs)	PD-1/PD L-1 inhibitors Inhibitory receptor CD152 (CTLA-4)
a) Pembrolizumab b) Nivolumab c) Atezolizumab, Avelumab d) Ipilimumab	
B) Antibody drug conjugate	Combines with Tissue factor causing microtubular damage
tftv/ Tisotumab Vedotin	
C)Therapeutic vaccines & Adoptive T cell therapies	Induce T cell response-CD 4 & CD 8 against HPV E6 and E7 oncoproteins
a) Therapeutic vaccines -AXAL b) Adoptive t cell therapies -Tumour infiltrating T cells -Genetically engineered T-cell therapy	Immune response against HPV E6 and E7 oncoproteins

Vascular endothelial growth factor (**VEGF**) is a protein that helps tumours in angiogenesis**.** These targeted drugs are called angiogenesis inhibitors that stop VEGF from working and block this new blood vessel growth.

EGFRs (Epidermal growth factor receptor) are over expressed in cervical cancer and is important in HPV16 mediated malignant transformation of keratinocytes.

Protein kinases transfer a γ-phosphate group from ATP to serine, threonine, or tyrosine residues. Many of these kinases are associated with human cancer initiation and progression. The recent development of small-molecule kinase inhibitors for the treatment of cervical cancer has proven successful in clinical therapy.

HPV E6 and E7 proteins are the biomarkers of a cervical cancer cell and are the ones driving the cancer progression disruption of p53- the guardian of the genome and Rb gene. Monoclonal antibodies, therapeutic vaccines & Adoptive T cell therapies represent a novel potential approach against the actions of these high risk-HPV E6 and E7 oncoproteins.

Immune checkpoints are critical to maintain tolerance against autoimmunity in physiologic conditions. **PD-1** is a transmembrane protein and expressed in B and T immune cells. The interaction of PD-1 and its receptor PD-L1 leads to blockage of T cell activation. More than 90 % cervical cancers are HPV related and there is up regulation of PD-L1 expression in tumour cells by E5, E6, E7 oncoproteins. While PD-L1 expression is rare in normal cervical tissue, it is present in around 50% of cervical cancer T cells. Upregulation of PD-L1 expression in tumour cells leads to increased binding and inhibition of PD1 receptors on T cells. This interaction results in tolerance of tumour antigens by major histocompatibility complex molecules and turns off the anti-tumour immune response. In addition, up regulation of PD-L1 expression causes release of tumour permissive T helper cell type 2 cytokines in the tumour micro environment. PDL-1 inhibitors break this cycle and enhance the immune response against tumour cells.

Similarly, Cytotoxic T lymphocyte-associated antigen-4 **(CTLA-4)** is a membrane glycoprotein expressed by activated effector T cells (Teffs) and participates in the repression of T cell proliferation, cell cycle progression and cytokine production.

Thus, immune check point inhibitors activate the T cells against the tumour cells.

Antibody-drug conjugate (ADC) is a monoclonal antibody linked to a chemotherapy drug. Tisotumab vedotin-tftv. This ADC has an antibody that targets **tissue-factor protein** on cancer cells. It acts like a homing signal by attaching to the TF protein bringing the chemo directly to the cancer cell.

Clinical Trials with Modalities of Target therapy

I. Antiangiogenetic Inhibition

Bevacizumab and other anti-angiogenesis agents-VEGFs have emerged as therapeutic targets for advanced cervical cancer. Bevacizumab is a recombinant humanised monoclonal antibody against VEGF-A and prevents angiogenesis. Phase III GOG 240 trial

showed that addition of bevacizumab (15mg/kg) to platinum and taxane based chemotherapy in first line setting of persistent, recurrent or metastatic cervical cancer is associated with modest overall survival (OS) benefit of 4 months without affecting the quality of life(16.8 months vs 13.3 months; p=0.007). One has to be vigilant for the side effects of bevacizumab viz hypertension, thromboembolic events, and gastrointestinal perforation, however in this series no major event was noticed. Systematic review & meta-analysis of 19 trials (2017) for persistent, recurrent and metastatic cervical cancer concluded that there is a trend towards increased OS for the addition of bevacizumab to cisplatin/paclitaxel or topetican/paclitaxel when compared with all other non-bevacizumab containing regimens.

Bevacizumab containing regimens are considered Category 1 option for treating persistent, recurrent, and metastatic cervical cancer but the additional cost of this treatment in our country should always be considered. (Box 1)

II. Epidermal growth factor receptor (EGFR) targeted treatment

Multiple phase II trials using EGFR antagonists such as erlotinib, gefitinib and cetuximab in recurrent cervical cancer did not show benefit over standard of care. Combinations of two types of drugs with different mechanisms (EGFR/HER-2 inhibitors with multitasked tyrosine kinase inhibitor of VEGFRs) also did not result in major benefit over standard care, rather had increased toxicity.

III. Immunotherapy

A) Immune Checkpoint Inhibitors (ICIs)

i) PD-1/PD-L1 inhibitors

Important drugs in this context are anti PD-1 (pembrolizumab, nivolumab); anti cytotoxic T lymphocyte antigen (CTLA-4) – Ipilimumab.

a) Pembrolizumab is monoclonal antibody that binds to PD 1 and inhibits the PD-L1 pathway. KEYNOTE 158, a phase II trial evaluated pembrolizumab as a single agent therapy, 200 mg IV 3 weekly in patients with advanced solid tumours, CPS >1 and progressive disease following standard treatments. (CPS is ratio of PD-L1 positive cells to total number of tumour cells x100). Drug was used till 2 years or patient had progressive disease or intolerable toxicity. There were 77 pre-treated cervical cancer patients & objective response rate (ORR) was 14.3% (95%CI, 7.4-24.1). Based on these findings, the drug was given accelerated approval for the subset of patients with this unmet need. Keynote 826 is A Phase 3 Randomized, double-blinded, Place bo- Controlled Trial of 'Pembrolizumab (MK-3475) Plus Chemotherapy' Versus 'Chemotherapy Plus Placebo' for the First-Line Treatment of Persistent, Recurrent, or Metastatic Cervical Cancer. It was observed that progression-free and overall survival significantly longer with pembrolizumab than with placebo among patients with persistent, recurrent, or metastatic cervical cancer who were also receiving chemotherapy with or without bevacizumab. *Pembrolizumab along with cisplatin/paclitaxel with or without Bevacizumab is first line treatment for persistent, recurrent, and metastatic cervical cancer in patients with PD-L1 receptors***.** (NCCN guidelines 2022)

b) Nivolumab is another monoclonal antibody with high affinity for PD-1. The drug allows tumour & E7 antigen specific T cell proliferation along with cytokine release. The Checkmate 358 phase I/II trial used Nivolimab 240 mg every two weeks until progression of disease or unacceptable adverse events in persistent, recurrent and metastatic cancer cervix. Out of 19 patients, OR in phase 1 cohort was 26.3% with a median follow up of 31 weeks. This drug is recommended as one of the second line single agent therapy in such cases.

c) CTLA-4 inhibitor-(cytotoxic lymphocyte antigen-4)

While PDL-1 inhibition has shown promising results in cancer therapy, combination approaches that target both PD-1 and CTLA-4 pathways have also been employed. The combination of ipilimumab, a CTLA-4 inhibitor, and nivolumab has shown good efficacy and is FDA approved for the treatment of melanoma. However, combination of these two drugs did not show good results in cancer cervix when it

was given in metastatic or recurrent cervical cancer patients who had progression after at least one line of platinum chemotherapy with pelvic radiotherapy.

B) Antibody drug conjugate – tftv/ tisotumab vedotin

A recent phase 2 trial revealed 24 % ORR with this drug after treatment of patients with persistent, recurrent or metastatic disease. The antibody targets the protein tissue factor which is highly prevalent in cervical cancer. This in turn results in intracellular microtubular damage. Other multiple immune mechanisms also play a role in its effectiveness. One fourth of patients did have grade 3 or 4 toxicity. This results in ocular side effects but maintains quality of life. A Phase 3 trial is ongoing and this drug got FDA approval in September 2021. NCCN guidelines recommend its use (category 2A) as second line single agent therapy for persistent, recurrent and metastatic cancer cervix.

C) Vaccines and adoptive T cell transfer therapies

a) Therapeutic Vaccines: Many trials have been done for therapeutic vaccination in cancer cervix. Two important aspects of vaccine are; the availability of immunogenicity antigen to produce a T cell response and a vaccine vector which acts as a platform for this. The HPV oncogenes E6 & E7 are expressed strongly in cervical cancer and are ideal antigens for the development of a therapeutic vaccine.

Vaccine vector can be cellular component such as dead cancer cells, bacteria, viral vectors, or peptides, DNA or RNA. Inactivated bacterial *Listeria monocytogenes* has been used as vector in AXAL, which stimulates a CD4 and CD8-mediated adaptive immune response targeting HPV-infected cells. Initial phase I data showed that the vaccine was well tolerated, although all patients were noted to have a flu-like syndrome, which ultimately did not require prescription treatment. Two phase II trials have been completed. The GOG phase II study enrolled 50 patients with metastatic disease whose disease had progressed on at least one prior systemic therapy and administered three doses of the vaccine. The 12-month overall survival was 38%, which represented an improvement compared with historical controls. In India, 110 patients with recurrent disease were randomized to three to four doses of AXAL with or without weekly cisplatin 40 mg/m2. More than a third of patients had stable disease or responses (including five complete responses) and 2- year overall survival was 18% across both treatment arms. The addition of cisplatin did not appear to improve outcomes compared with AXAL alone. Based on this encouraging data, a larger phase III trial was initiated in the definitive setting (NCT02853604). Unfortunately, the trial was closed prematurely in 2019 and no results have been presented or published to date. Results from these clinical trials were not the basis for this decision to close the study, nor was the safety. The trial recently underwent its third Independent Data Monitoring Committee (IDMC) review with no safety issues noted. The company plans to unblind the AIM2CERV clinical data generated to date and anticipates submitting these data for publication.

b) Adoptive T cell therapies– these novel therapies have shown promising results in phase I and II trials.

i) T cells are cultured from samples of a metastatic tumour or draining lymph node and tested for activity against E6 and E7 proteins. Cultures that show high T-cell content and purity with good reactivity are further propagated and then administered to the patient in a single-dose IV infusion after preparatory lymphocyte depleting chemotherapy.

ii) Genetically engineered T-cell therapy entails isolation of patient's peripheral mono- nuclear blood cells and then uses a retrovirus encoding HPV-related genes to engineer the T cells to target infected cells. Engineered cells are propagated over several weeks and then infused back into the patient after preparative chemotherapy.

IV. The possible synergies between immunotherapy and radiation therapy are being explored in clinical trials and it might be the future protocol for treatment of cervical cancer.

There are temptations to use immunotherapy in terminally ill patients when no effective therapy is available (Desperation Oncology). With advances in molecular biology and therapeutics every case will find its appropriate drug in near future.

Conclusions

Target therapy is the future of chemotherapy and has moved from blanket therapy to personalised medicine.

It is specific, highly effective, less toxic and maintains quality of life. Cost is limiting factor in India.

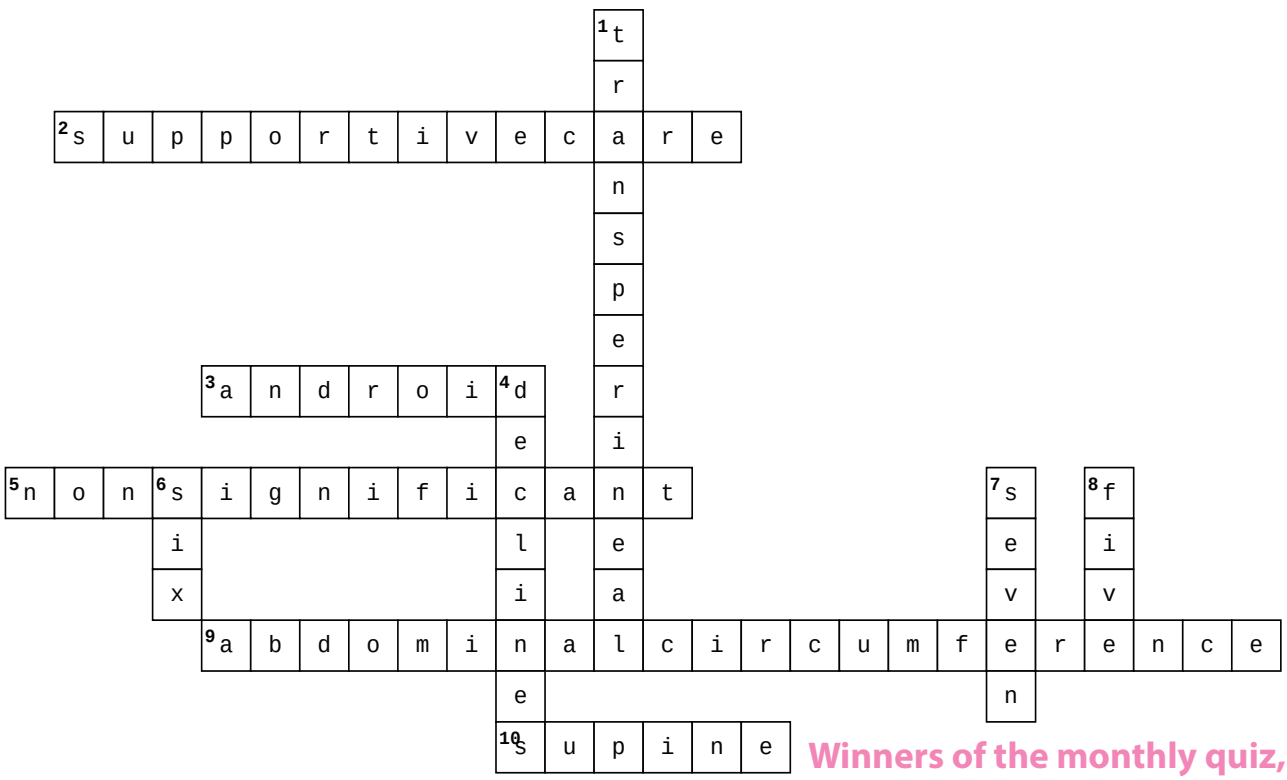
Bevacizumab has been included in upfront treatment of persistent, recurrent, and metastatic cervical cancer which is not amenable to surgery or radiotherapy.

Pembrolizumab along with cisplatin/paclitaxel with or without Bevacizumab is first line treatment for persistent, recurrent, and metastatic cervical cancer in patients with PD-L1 receptors.

Recommended Reading

1. Abu-Rustum NR, Yashar CM, Bean S et al. NCCN Guidelines Insights: Cervical Cancer, Version 1.2020. J Natl Compr Canc Netw. 2020 Jun;18(6):660-666. doi: 10.6004/jnccn.2020.0027. PMID: 32502976
2. Odiase O, Noah-Vermillion L, Simone BA and Aridgides PD (2021) The Incorporation of Immunotherapy and Targeted Therapy Into Chemoradiation for Cervical Cancer: A Focused Review. Front. Oncol. 11:663749. doi: 10.3389/fonc.2021.663749
3. .Sherer MV, Kotha NV, Williamson C, et al. Advances in immunotherapy for cervical cancer: recent developments and future directions. Int J Gynecol Cancer 2022;32:281
4. Schmidt WM, Battista M, Schmidt M et al. Efficacy and Safety of Immunotherapy for Cervical Cancer—A Systematic Review of Clinical Trials. Cancers (Basel). 2022 Jan; 14(2): 441. PMCID: PMC8773848
5. CCN guidelines for cervical cancer V.1 2022 "Cervical_1_2022_061121.pdf" http//www.NCCN.org

Answer key of Quiz of September 2022



Winners of the monthly quiz, September Issue 2022

1. Dr Divya Meena
2. Dr Vijaita Thakur
3. Kajal Kesharwani

Abnormal Pap smear and Cervical Cancer in Pregnancy: What to do? When to do?

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INTRODUCTION

Cervical cancer is the second leading cause of cancer deaths among women in India with age-standardized incidence and mortality rates of 22 and 12.4 per 100,000 women per year OR 0.8 to 1.5 cases per 100,000 births making it the most common malignancy during pregnancy.[1] Twenty-five per cent of all global deaths due to cervical cancer occur in India. The reason for this difference is lack of effective screening and access to timely treatment. However, pregnancy provides an opportunity to early screening being the first access to healthcare for many women in our country. At the time of diagnosis, 1 to 3 percent of women are either pregnant or postpartum.[2,3] Approximately one-half of these cases are diagnosed prenatally, and the other half are diagnosed in the 12 months after delivery.

Pregnancy does not change the natural history of human papilloma virus (HPV) and pregnant patients are considered to have similar rates of progression to cancer as their nonpregnant counterparts. Abnormal screening results should be managed using the same risk/ clinical action thresholds as those established for nonpregnant individuals. Of note, up to 5% of cervical intraepithelial neoplasia I-II may progress to invasive cancer during gestation.[4]

PHYSIOLOGICAL CHANGES AND SCREENING IN PREGNANCY

Pregnancy provides many women the opportunity for having their first ever contact with healthcare facilities and hence screening for Ca cervix may be offered to all pregnant women. Previous studies have shown that the accuracy of cervical cytological diagnosis in pregnancy is similar to that in the non-pregnantstate.[5,6] However, recent studies have shown that changes in maternal estrogen and progesterone levels lead to glandular hyperplasia of cervical mucosa, migration of squamous columnar junction, active proliferation of basal cells, irregular cell morphology, and enlargement of nuclei, which are easily misdiagnosed as highly squamous intra-epithelial lesions or even invasive cancer.

Screening can be done by 'three-step model' including cervical cytology, colposcopy and cervical biopsy.

Special recommendations for screening in pregnancy[7]:

- Using broom stick rather than cytobrush, moistened cotton swab for taking cytology (as it may disturbs the endocervical canal).
- Avoid endocervical curettage, endometrial biopsy.
- Diagnostic excisional procedure or repeat biopsy is recommended only if cancer is suspected based on cytology, colposcopy, or histology.
- If histologic HSIL (CIN 2 or CIN 3) is diagnosed at the first colposcopy examination during pregnancy, surveillance colposcopy and testing (diagnostic cytology/ HPV depending on age) is preferred every 12 to 24 weeks, but deferring colposcopy to the postpartum period is acceptable. Treatment is not recommended.
- Postpartum colposcopy should be delayed until 4 weeks postpartum.

Reporting of Pap Smear in Pregnancy:

Overall, the rate of significant cytological abnormalities among obstetrical patients has been reported to be 5 to 8 percent and is similar to that of the nonpregnant population.[8]

It is important to mention about the pregnancy status on the cytology forms to facilitate accurate reporting by an experienced pathologist and avoid false positive or false negative reporting.[9] As transformation zone expands in early pregnancy, it is easier to sample endocervical cells which may act as surrogate marker for the

adequacy of the sample obtained.

INDICATIONS OF COLPOSCOPY IN PREGNANCY[7]

The indications of colposcopy include

1. Post-coital bleeding or abnormal vaginal bleeding (after excluding obstetric causes)
2. Cervical abnormality or suspicious lesions noted during routine gynaecological examination
3. Abnormal cytology meeting the criteria for colposcopic evaluation[10]
   - ASC-US (atypical squamous cells of undetermined significance) on Cervical cytology: patients with HPV-positive can be re-examined at 6 months postpartum
   - LSIL: Patients with low-grade squamous intraepithelial lesion
   - ASC-H: Atypical squamous cells whereby high-grade squamous intraepithelial lesion cannot be excluded
   - HSIL/AGC: Pregnant women with high-grade squamous intraepithelial lesions, atypical glandular cells, and above.

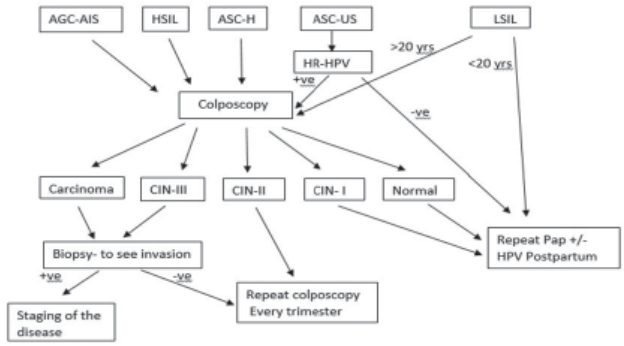
OBSTETRIC CONCERNS

Cervical curettage during pregnancy must be avoided, whereas cervical biopsy has not been shown to increase the incidence of complications during pregnancy, abortion rate, or premature delivery rate.[11,12]

ABNORMAL PAP SMEAR IN PREGNANCY:

Pregnancy-associated cancer pose a challenging situation owing to ethical dilemma of managing two lives together with an underlying malignancy. The complexities involved in managing pregnant patients with cervical cancer depends on many factors, such as malignant staging of tumor, gestational age, and fetal development. Multidisciplinary teams including gynecologist, oncologist, obstetrician, pathologist, neonatologist, medical oncologist and intensivist. Management outline is depicted in table-1.

Table 1: Management of the abnormal Pap smear and CIN in pregnancy:



TREATMENT OF CERVICAL INTRAEPITHELIAL LESION (CIN)

1. LSIL (CIN 1): review after 6 weeks postpartum
2. HSIL (CIN 2/3) cervical cytology and colposcopy should be re-evaluated at 6 weeks postpartum and every 12 weeks after excluding invasive cervical cancer.[6]
3. Repeat biopsy should be taken if any evidence of disease progression or invasive lesion found in postpartum examination.
4. If high suspicion of invasive cervical cancer present: offer diagnostic cervical loop electrosurgical excision (LEEP) or cervical cold knife conization (CKC).[13,14]

CERVICAL CANCER DURING PREGNANCY:

CLINICAL PRESENTATION

Most cases of cervical cancer in reproductive age group are detected on routine screening. The overall performance of PAP test do not appear to differ significantly between pregnant and non-pregnant women.[6]

The presenting signs and symptoms during pregnancy depend upon clinical stage and size of the lesion.

Stage IA: all are asymptomatic

Stage IB: 50 percent asymptomatic, abnormal vaginal bleeding or discharge

Advanced disease: pelvic pain, sciatica-type leg pain, flank pain, chronic anemia, and shortness of breath

Many of these symptoms mimic the physiological changes of pregnancy, which may lead to delay in diagnosis of the underlying malignancy.[15]

STAGING: Same as in non-pregnant patients

DIAGNOSTIC EVALUATION

The diagnosis is based on histopathological evaluation of the biopsied specimen. It is important to refer the patient to gynaeological oncologist for optimal staging and management.

PHYSICAL EXAMINATION:

- Constitutes key element of staging
- Includes assessment of primary tumor, uterus, vagina, parametria, groin, right upper quadrant, and supraclavicular nodes.
- Limitations during pregnancy: physiological changes of pregnancy such as ectropion, stromal edema, and ripening may resemble early neoplasia. The normal decidual reaction of the cervix may resemble carcinoma.

IMAGING IN PREGANCY:

- Imaging involved in FIGO staging (2018): chest and skeletal radiographs, intravenous pyelogram (IVP), and barium enema.
- Other imaging: Computed Tomographic (CT), Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET), and lymphangiograms may be used but not necessary.
- Pregnancy concerns: balancing the need for accurate staging using imaging and simultaneously limiting the fetal exposure.
- A chest x-ray (with abdominal shielding): to evaluate for pulmonary metastasis.
- For stage IA and microscopic/very small stage IB (<1 cm): urinary tract imaging may be omitted.
- For larger stage IB1, bulky stage IB2, or more advanced disease and/or higher-risk histology (adenocarcinoma, small cell carcinoma): USG or MRI abdomen and pelvis for patient counselling and management plan.

MANAGING CERVICAL CANCER IN PREGNANCY:

Challenges:

- A careful multidisciplinary team approach is required and should take into account the desires of the pregnant patient (and her family) regarding preservation of the pregnancy.
- Ethical dilemma regarding desire to continue pregnancy versus fear of disease progression.

An outline to approach to manging cervical cancer in pregnancy has been outlined in table 2 and table 3

Table 2: approach to managing ca cervix in women not desirous of continuing pregnancy

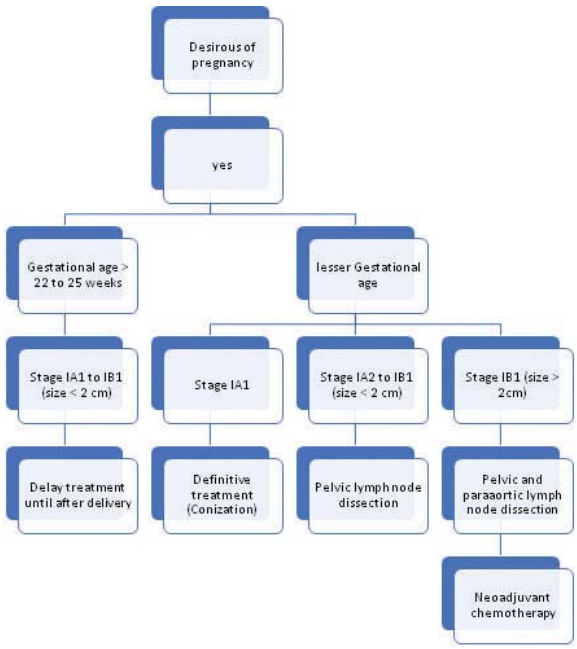


Table 3: Approach to managing ca cervix in women desirous to preserve pregnancy

- Stage IA to IB1 (< 2 cm): consider delaying

treatment by six to eight weeks after delivery if diagnosed in second trimester and beyond.[16]

- Stage ≥ IB2: offer definitive treatment. However, if patient willing to preserve pregnancy, consider neoadjuvant chemotherapy (NACT) until delivery.[17]
- Immediate and definitive management regardless of stage may be considered in following settings:
  a. Disease progression during pregnancy
  b. Positive lymph nodes
  c. Patient not desirous to continue the pregnancy

FOLLOW-UP DURING PREGNANCY:

- Follow-up during pregnancy is important to determine disease progression.
- Stage IA1: clinical examination and colposcopy in each trimester during pregnancy.
- Patients on NACT: pelvic examination every three to four weeks during pregnancy. MRI without contrast may be used to rule out disease progression.
- Role of maternal-fetal medicine specialist: for close maternal surveillance and monitoring of fetal growth and well-being.

Role of Neoadjuvant Chemotherapy[11]:

a. Overall response rate of upto 90 percent and complete response rate of upto 62.5 percent has been observed in one review of 50 patients.

b. The median gestation age at diagnosis was 19 weeks and platinum based chemotherapy was administered at three weeks interval upto 33 weeks gestational age.

c. Survival reported:

Stage IB1	94 percent
Stage IB2	70 percent
Stage >IB	70 percent

Cisplatin plus paclitaxel delivered every three weeks for upto six weeks continued upto 34 weeks followed by delivery at term.

LYMPHADENECTOMY IN PREGNANCY

- Patients diagnosed with high-risk (node-positive) disease should be counselled about the importance of initiating immediate definitive therapy.[18]
- Selected patients who wish to continue pregnancy with high risk of lymph node metastases, staging lymphadenectomy may be done using extraperitoneal or laparoscopic approach.[19-21]

TERMINATION OF PREGNANCY

- The decision to terminate the pregnancy should include consideration of stage of disease, treatment options, patient preferences, and fetal viability.
- Early-stage disease: Radical hysterectomy with fetus in situ with preservation of ovaries whenever possible.
- Advanced Disease: Offer definitive treatment as in non-pregnant patient.
- Timing of delivery: individualized based on the gestational age, stage of cervical cancer, disease progression on follow-up. Term delivery at ≥ 37 weeks and ideally at 39 weeks must be considered unless other obstetric indication for earlier termination arises.
- MODE OF DELIVERY: Women with stage IA1 and IA2 cervical cancer can proceed with a vaginal delivery with caesarean section reserved for obstetric indication. Avoid episiotomy wherever possible.[22]Avoid vaginal delivery in stage IB1 or higher and planned caesarean at term must be considered.[23,24]
- VERTICAL TRANSMISSION: Rare cases of vertical transmission has been observed with possibility of transplacental (hematologic) and/or aspiration of tumor-contaminated fluids into the fetal lungs during vaginal delivery. Two cases of pediatric lung cancer were diagnosed in newborns delivered vaginally to women with ca cervix. Identical pathological DNA mutations were detected in maternal and pediatric tumor histologies.[25]

EFFECT OF CERVICAL CANCER ON PREGNANCY

The effect of ca cervix on pregnancy is not very clear and observation is based on few

retrospective studies.

REFERENCES

1. Smith LH, Danielsen B, Allen ME, Cress R. Cancer associated with obstetric delivery: results of linkage with the California cancer registry. American journal of obstetrics and gynecology. 2003 Oct 1;189(4):1128-35.
2. Nguyen C, Montz FJ, Bristow RE. Management of stage I cervical cancer in pregnancy. Obstetrical & gynecological survey. 2000 Oct 1;55(10):633-43.
3. Smith LH, Dalrymple JL, Leiserowitz GS, Danielsen B, Gilbert WM. Obstetrical deliveries associated with maternal malignancy in California, 1992 through 1997. American journal of obstetrics and gynecology. 2001 Jun 1;184(7):1504-13.
4. Hecking T, Abramian A, Domröse C, Engeln T, Thiesler T, Leutner C, Gembruch U, Keyver-Paik MD, Kuhn W, Kübler K. Individual management of cervical cancer in pregnancy. Archives of gynecology and obstetrics. 2016 May;293(5):931-9.
5. Morice P, Uzan C, Gouy S, Verschraegen C, Haie- Meder C. Gynaecological cancers in pregnancy. Lancet. 2012;379(9815):558-569.
6. Morimura Y, Fujimori K, Soeda S, et al. Cervical cytology during pregnancy: comparison with non-pregnant women and manage- ment of pregnant women with abnormal cytology. Fukushima J Med Sci. 2002;48(1):27-37.
7. Beharee N, Shi Z, Wu D, Wang J. Diagnosis and treatment of cervical cancer in pregnant women. Cancer Med. 2019;8(12):5425-5430. doi:10.1002/cam4.2435
8. Van Calsteren K, Vergote I, Amant F. Cervical neoplasia during pregnancy: diagnosis, management and prognosis. Best Practice & Research Clinical Obstetrics & Gynaecology. 2005 Aug 1;19(4):611-30.
9. Morimura Y, Fujimori K, Soeda S, et al. Cervical cytology during pregnancy: comparison with non-pregnant women and manage- ment of pregnant women with abnormal cytology. Fukushima J Med Sci. 2002;48(1):27-37.
10. Li T, Wang J, Song F. Progress in the diagnosis and treatment of gynecological malignant tumors during pregnancy. Cancer Progression. 2018;16(13):1589-1592, 1615.
11. ain AG, Higgins RV, Boyle MJ. Management of low-grade squamous intraepithelial lesions during pregnancy. Am J Obstet Gynecol. 1997;177(2):298-302.
12. Schaefer K, Peters D, Aulmann S, Sohn C, Eichbaum M. Value and feasibility of LLETZ procedures for pregnant women with sus- pected high-grade squamous intraepithelial lesions and microinva- sive cervical cancer. Int J Gynaecol Obstet. 2012;118(2):141-144
13. Siegler E, Lavie O, Amit A, Vaknin Z, Auslander R, Blumenfeld Z. Should the risk of invasive cancer in pregnancy and the safety of loop electrosurgical excision procedure during the first 15 weeks change our practice?. J Low Genit Tract Dis. 2017;21(4):299-303.
14. Robova H, Rob L, Pluta M, et al. Squamous intraepithelial lesion- microinvasive carcinoma of the cervix during pregnancy. Eur J Gynaecol Oncol. 2005;26(6):611-614.
15. Lee RB, Neglia W, Park RC. Cervical carcinoma in pregnancy. Obstetrics and Gynecology. 1981 Nov 1;58(5):584-9.
16. Van der Vange N, Weverling GJ, Ketting BW, Ankum WM, Samlal R, Lammes FB. The prognosis of cervical cancer associated with pregnancy: a matched cohort study. Obstetrics & Gynecology. 1995 Jun 1;85(6):1022-6.
17. Germann N, Haie-Meder C, Morice P, Lhomme C, Duvillard P, Hacene K, Gerbaulet A. Management and clinical outcomes of pregnant patients with invasive cervical cancer. Annals of oncology. 2005 Mar 1;16(3):397-402
18. Amant F, Halaska MJ, Fumagalli M, Steffensen KD, Lok C, Van Calsteren K, Han SN, Mir O, Fruscio R, Uzan C, Maxwell C. Gynecologic cancers in pregnancy: guidelines of a second international consensus meeting. International Journal of Gynecologic Cancer. 2014 Mar 1;24(3).
19. Van Calsteren K, Hanssens M, Moerman P, Orye G, Bielen D, Vergote I, Amant F. Successful conservative treatment of endocervical adenocarcinoma stage Ib1 diagnosed early in pregnancy. Acta obstetricia et gynecologica Scandinavica. 2008 Jan 1;87(2):250-3.
20. Alouini S, Rida K, Mathevet P. Cervical cancer complicating pregnancy: implications of laparoscopic lymphadenectomy. Gynecologic oncology. 2008 Mar 1;108(3):472-7.
21. Hertel H, Possover M, Kühne-Heid R, Schneider A. Laparoscopic lymph node staging of cervical cancer in the 19th week of pregnancy. Surgical endoscopy. 2001 May;15(3):324-.
22. VandenBroek NR, LOPES AD, Ansink A, Monaghan JM. "Microinvasive" adenocarcinoma of the cervix implanting in an episiotomy scar. Gynecologic oncology. 1995 Nov 1;59(2):297-9.
23. Baloglu A, Uysal D, Aslan N, Yigit S. Advanced stage of cervical carcinoma undiagnosed during antenatal period in term pregnancy and concomitant metastasis on episiotomy scar during delivery: a case report and review of the literature. International Journal of Gynecologic Cancer. 2007 Sep 1;17(5).
24. Tewari K, Cappuccini F, Gambino A, Kohler MF, Pecorelli S, DiSaia PJ. Neoadjuvant chemotherapy in the treatment of locally advanced cervical carcinoma in pregnancy: a report of two cases and review of issues specific to the management of cervical carcinoma in pregnancy including planned delay of therapy. Cancer: Interdisciplinary International Journal of the American Cancer Society. 1998 Apr 15;82(8):1529-34.
25. Arakawa A, Ichikawa H, Kubo T, Motoi N, Kumamoto T, Nakajima M, Yonemori K, Noguchi E, Sunami K, Shiraishi K, Kakishima H. Vaginal transmission of cancer from mothers with cervical cancer to infants. New England Journal of Medicine. 2021 Jan 7;384(1):42-50.

Risk Management- Documentation

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In medicine documentation is a term relating to a patient care medical record. It is a form of communication, a document of service and most importantly a legal document.

Good documentation leads to clear communication. Failure to document relevant data is itself considered a significant breach of and deviation from the standard of care.[1–3] "If it was not documented it was not done".

Protection from legal risk is not the only reason for documentation in healthcare. The patient's records serve as a record of the continuum of care of the patient and are valuable in emergency care, quality assurance and research.

Types of Documentation in Healthcare

The documents in healthcare can be classified as Non-clinical and Clinical.

1. **Non-clinical documentation**
   a. These are documents which are necessary for fulfilling statutory, regulatory and legal requirements as laid down by the government, and other competent regulatory and legal institutions.
2. **Clinical Documentation**
   a. Clinical documentation is that which covers the medical journey of a patient.
   b. This documentation contains the detailed history of the patient's presenting complaints, past medical, personal, social history; the clinical findings, the investigations advised, the results thereof, the most probable diagnosis, the medical decisions, the treatment plan, the follow-up and the progress and outcomes.

Clinical Medical Documentation

Clinical documentation is not confined to prescriptions, in patient records, nursing records, and discharge summary. The ambit of medical documentation is far reaching.

They can be tabulated as follows:

1. Handwritten clinical notes
2. Patient Information leaflets
3. Emails
4. Letters to and from other health professionals
5. OPD medical records
   a. Prescriptions
   b. Investigations and the results
   c. Treatment documents
   d. Referrals
   e. Follow-up advice
6. Screening Tests as per hospital policy e.g., COVID- 19
7. IPD medical Records
   a. Admission advice and reason
   b. Admission notes
   c. Doctors' notes
   d. Treatment orders
   e. Consents of various treatment plans
   f. Ward Round notes and Progress notes
   g. Operative notes
   h. Videotapes, photographs or any other media recording
   i. Physiotherapy notes
   j. Nursing notes
   k. Referral Notes
   l. Laboratory reports
   m. X-rays and other radiological documents
   n. Printouts from monitoring equipment
   o. Incident reports and statements
8. Discharge papers
   a. Advice on Discharge
   b. Follow-up advice
   c. Contact advice in case of any Emergency
   d. Medical Certificates

Core standards of Medical Record documentation

As per National Medical Commission

1. Each page in the record must contain the

patient's name or ID number, personal data e.g., age, sex, marital status, address, and telephone numbers.

2. Document history and duration of patient's present Illness and concerns, patient's allergies (failure to document can have serious/ fatal consequences).
3. Document past medical history, social history and family history. Personal history should include the use of cigarettes, alcohol and substance abuse.
4. The current medication that the patient is taking must be documented.
5. Physical examination - General examination and local complaint specific examination must be done and the significant positive and negative clinical findings must be documented clearly. Proper documentation of this aspect is found to be lacking in a large number of cases.
6. Document the working diagnosis and treatment plan.
7. Document investigations advised.
8. Document advice for admission (if given) after necessary counselling and informed consent for the management planned.
9. Document treatment plan clearly and communicate it to the relevant members of the team and the administration.
10. Follow-up and contact advice in cases of any emergency.
11. During patient care any videos, tape-recordings of telephone conversations and text messages should be recorded.

Important aspects of notes

1. Entries are to be made immediately or as soon as possible after care is given reduces risk of forgetting details
2. Entries should all be dated, and records written legibly and methodically
3. Details of writer of notes and details of the treating Consultant / team must be mentioned
4. All results of investigations should be checked and initialled by the Consultant or designated member of the team,
5. Informed consent to be taken after counselling
6. Signature is essential in documentation. It can be handwritten or can be a unique electronic signature
7. If attending a referral - advice should be discussed with the primary consultant and documented
8. Discussion of treatment options and response of the patient must be documented e.g.

a. Treatment plan will be discussed further at a later visit after availability of records.

b. Patient will discuss at home and subsequently decide about the treatment plan

c. Refuses treatment plan and reasons for refusal

9. Notes should be without emotion, or any derogatory remarks
10. **Avoid abbreviations** – they can mean more than one thing e.g. PID for the Gynaecologist means Pelvic Inflammatory Disease but in Orthopaedics PID is Prolapsed Intervertebral Disc; MS - can mean - Meconium staining, Mitral Stenosis or even Multiple Sclerosis. Only standard abbreviations are to be used.
11. Addenda - when required one must document the time and signature and also communicate verbally with the staff.
12. If the primary notes are written later, document that it was written in retrospect, with the current date and time
13. Mistakes
    a. should be corrected it with a single strikethrough with signature and date.
    b. Do not insert, use little arrows, or write between lines etc. The original and correction should be clear.
14. For making changes in a pre-existing entry – the new entry should have the date and current time, and then write the correction with reasons for change.
    1. Consultation and abnormal laboratory and imaging study results should be clearly recorded for follow-up plans.
    2. All abnormal reports are documented, patient informed and counselled. This

Interaction is to be documented.

3. Risks of procedures and investigations should be explained to the patient and documented.
4. An immunization record (for children) is up to date, or an appropriate history has been made in the medical record (for adults).
5. Document that preventive screening and services are offered in accordance with the organization's practice guidelines e.g., screening for COVID-19.

A good cclinical documentation should be accurate, complete, specific and legible

Salient points of Guidelines on documentation by the National Medical Commission

1. Date and time are a must.
2. Handwriting should be legible and meaning of document should be clear to others.
3. Treatment plans should be clear, and records should identify risks or problems that have arisen and the action plan.
4. Use professional judgement to decide relevant facts to be recorded and do not falsify records.
5. Do not alter or destroy any records unless authorised to do so.
6. In you need to alter your own or another healthcare professional's records, you must give your name and job title, and sign and date the original documentation. You should make sure that the alterations you make, and the original record, are clear and auditable.
7. Photocopied and scanned records should be clear and readable.

Who will have access to your records?

1. While writing the record keep in mind who all will be reading the documents

This will include –

a. Other members of the treatment team,

b. Other consultants and colleagues covering the clinician on vacation or who is not available.

c. Insurance companies

d. Members of professional standards review organizations

e. Internal auditors and accrediting bodies (e.g. NABH or other accrediting bodies)

f. Lawyers and courts

g. Consumer forums

h. Patients themselves can for the records.

Writing notes with this thought in mind will help achieve clarity and avoid objectionable remarks.

Confidentiality of documents

1. This must be maintained at all costs.
2. Follow local policy and guidelines when using records for research purposes.
3. Do not discuss patient care and details in places where you might be overheard e.g., elevators, common areas etc.
4. Do not leave records, either on paper or on computer screens, where they might be seen by unauthorised staff or members of the public.
5. You should not take or keep photographs of any person, or their family, which are not clinically relevant.

Access

1. Patients should be told that information on their health records may be seen by other people or agencies involved in their care.
2. Patients have a right to ask to see their own health records. You should be aware of the procedures regarding this request.
3. If you have any problems relating to access or record keeping, such as missing records or problems accessing records, you should escalate the matter to the respective authority and document this fact.
4. Do not access the records of any person, or their family, to find out personal information that is not relevant to their care.

Disclosure

1. Information that can identify a patient must not be used or disclosed for purposes other than healthcare without the individual's explicit consent, except when required by law.

2. Under common law, you are allowed to disclose information if it helps prevent, detect, investigate or punish serious crime or if it will prevent abuse or serious harm to others.
3. Learn how to use the information systems and tools that are available to you in your practice for documentation.

Personal and professional knowledge and skills

You are dutybound to keep up to date with, and adhere to, relevant legislation, case law and national and local policies relating to information and record keeping. (National Medical Commission).

Some aspects of documentation need a special mention

Documenting a ward round

You must document the name of healthcare professionals, patient's family and relatives present at the time of the ward round.

Start with a summary of the main reason for admission, treatment plan and progress.

The steps of documentation can be remembered by the pneumonic **SOAP** (Theorised by larry weed 50 years ago). Other methods are also used.

The SOAP method

SOAP stands for Subjective, Objective, Assessment, and Plan.

- **Subjective**
  - o Document the patients' complaints, chronology, duration, intensity and concerns and feelings in a narrative form.
- **Objective**
  - o Document the objective observations that you make in the patient encounter. Stating that the "patient was sitting comfortably in bed having his/ her meal" is far more descriptive than mentioning the clinical parameters only.
  - o Document the clinical assessment and parameters.
  - o Document the recent lab results, fluid balance, catheters, urine output, IV fluids, diet etc.
- **Assessment**
  - After the subjective and objective assessment document the salient points and assess the patient's clinical progress.
  - This documentation can also be in a narrative form e.g., "*the patient is comfortable, the catheter has been removed, she has passed flatus and is tolerating a soft diet.*"
  - In patients in high dependency units and intensive care units or patients in active labour assessment should be more frequent. Any new developments should be documented for better communication with changing teams.
- **Plan**
  - o Management plans should be clearly documented.
  - o Document and convey all instructions regarding medication or changes, procedures planned and care to the relevant medical team .
  - o Any referrals should be clearly documented and conveyed verbally also.
  - o In case of likely discharge of the patient, the information is to be documented with the discharge advice written and to the family and hospital team.

Developing a checklist in ward rounds and note writing can improve overall compliance with documentation. According to Gordon Hale documentation improved from 45% to 89%. (MJ Quality Improvement Programme, Gordon Hale, Duncan McNab.

Documenting a family meeting

This discussion can be unstructured and difficult to document. It is useful to have structured family meeting forms which leads to easier documentation and ensures no important issues are missed in discussions.

Steps of documenting family meetings:

1. Document names of all the people present in the meeting – medical staff, family and relatives of patient, translators, social workers.

All names and signatures should be obtained.

2. Video recording of this counselling and meeting is recommended in serious and difficult cases.
3. The points and issues to be discussed are mentioned clearly in sequence.
4. List, discuss and document each point as it is raised. Exact quotations of the family can be noted with quotation marks.
5. At the close of the meeting the agreements and conclusions reached regarding the treatment plan are documented.
6. The conclusions arrived at are to be documented and names and signatures of all present are obtained along with their relationship of the family and relatives to the patient.

Documenting a procedure

All procedures whether bedside or in the operating room are to be documented clearly. The documentation must include – consents, any medication or instruments used and finally the completion and outcome of the procedure.

Documenting a mistake in care

Mistakes might happen. Do not dismiss them or hide them. Document the condition of the patient after such an incident. An incident report must be raised and documented.

The discharge summary

The discharge summary should not be written casually. It is the most comprehensive document about patient care during admission.

It should have a structured format follow:

- **Principal diagnosis** – Reason for the admission
- **Co-morbidities** – These conditions resulted in a change to the patient's treatment, care or length of stay.
- **Complications** – conditions that arose during the admission and affected the patient's treatment and length of stay.
- **Procedures** – Surgical, non-operative, diagnostic, therapeutic procedures that required anaesthesia, sedation or injected contrast.
- **Discharge medication list –** clearly outline any medication changes that were made.
- **Discharge plan** –
  - o Must have clear instructions to be followed by the patient and the caregivers after discharge.
- Instruction for follow-up appointments and return to the hospital in case of any emergency.

Electronic Health records – A word of caution

These are important and convenient to use and can maintain records indefinitely.

1. Be aware of what is already there in the templates you use.
2. Be wary of "copy and paste" Mistakes often take place when such short cuts are employed.
3. Keep discharges professional
   a. Avoid caps lock and excessive use of bold typing.
   b. Do not use fancy fonts and colours.

Documenting a phone conversation

1. Keep a record of the phone conversation, name of person, relationship with patient, and points discussed should be documented.
2. Note the telephone number of the person if they need to be contacted again.
3. Do not disclose information about the patient over the phone to others.

Medical Documentation in Telemedicine

The **National Medical Commission** has outlined the details of Telemedicine documentation in Healthcare in Section 3.7.2 and 4.1.1.2. Some salient points are:

3.7.2 MAINTAIN DIGITAL TRAIL/ DOCUMENTATION OF CONSULTATION.

Maintain the following records/ documents for the period as prescribed from time to time:

3.7.2.1 Log or record of Telemedicine interaction (e.g., Phone logs, email records, chat/ text record, video interaction logs etc.).

3.7.2.2 Patient records, reports, documents, images, diagnostics, data etc. (Digital or non-Digital) utilized in the telemedicine consultation should be retained by the Registered Medical

Practitioner(RMP).

3.7.2.3 The RMP is required to maintain the prescription records.

4.1.1.2 Patient identification and consent must be confirmed. Consent is implied when a patient seeks a consultation.

In an emergency situation, the patient MUST be advised for an in-person interaction with a Registered Medical Practitioner at the earliest. The RMP, based on his/ her professional discretion may advise first aid, counselling and facilitate referral guidance.

Consent

This is a very important part of documentation.

1. The consents can be implied, informed, express, surrogate consent.
2. The consent should be person and procedure specific.
3. Informed consent should be taken from persons who can understand the procedure and the purpose and nature of the treatment, the consequences as well as the risks of the intervention, alternatives available and the prognosis in the absence of intervention.

Medical Certificates

1. Keep a record and details of certificates issued.
2. Patient must be examined before issuing of certificate.
3. No false certificates are to be given.

Retention of Records

As per the directive of the Ministry of health and Family Welfare vide Office memorandum dated 28/10/2014.

a. IPD to be digitised and kept indefinitely for further research purposes
b. Case sheets for 3 years
c. OPD Records - 3 years
d. Medicolegal cases – till the case is finally deposed off

1. Documents to be given to patient within 72 hours of their request
2. Assisted Reproductive Technology Regulation Act 2021 - Records must be kept for at least ten years after which the records must be moved to a central National Registry (as and when established). If the ART clinic is wound up during this period, the records must be transferred to the above Registry.

Medical documentation has expanded over the past decades. However, we must not overburden a busy clinician but should strive to make documentation structured and easily retrievable. Good documentation is the best defence in malpractice cases.

References

1. Catherine Moore. Writing SOAP Notes, Step-by-Step: Examples + Templates. Quenza website. https://quenza.com/blog/soap-note/. Updated April 13, 2021.
2. Gordon Hale, Duncan McNab. Developing a ward round checklist to improve patient safety. . PMID: 26734369 PMCID: PMC4645926 DOI: 10.1136/bmjquality.u204775.w2440 April 2015.
3. Gutheil TG, Appelbaum PS. Clinical Handbook of Psychiatry and the Law. Third Edition. Baltimore, MD: Lippincott, Williams, and Wilkins; 2000.
4. National medical Commission, https://www.nmc.org.in
5. Podder V, Lew V, Ghassemzadeh S. SOAP Notes. [Updated 2021 Sep 2]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan.
6. Thomas G. Gutheil. Fundamentals of Medical Record Documentation. Psychiatry (Edgmont). 2004 Nov; 1(3): 26–28. Published online 2004 Nov. PMCID: PMC3010959 PMID: 21191523.

Events held in September 2022

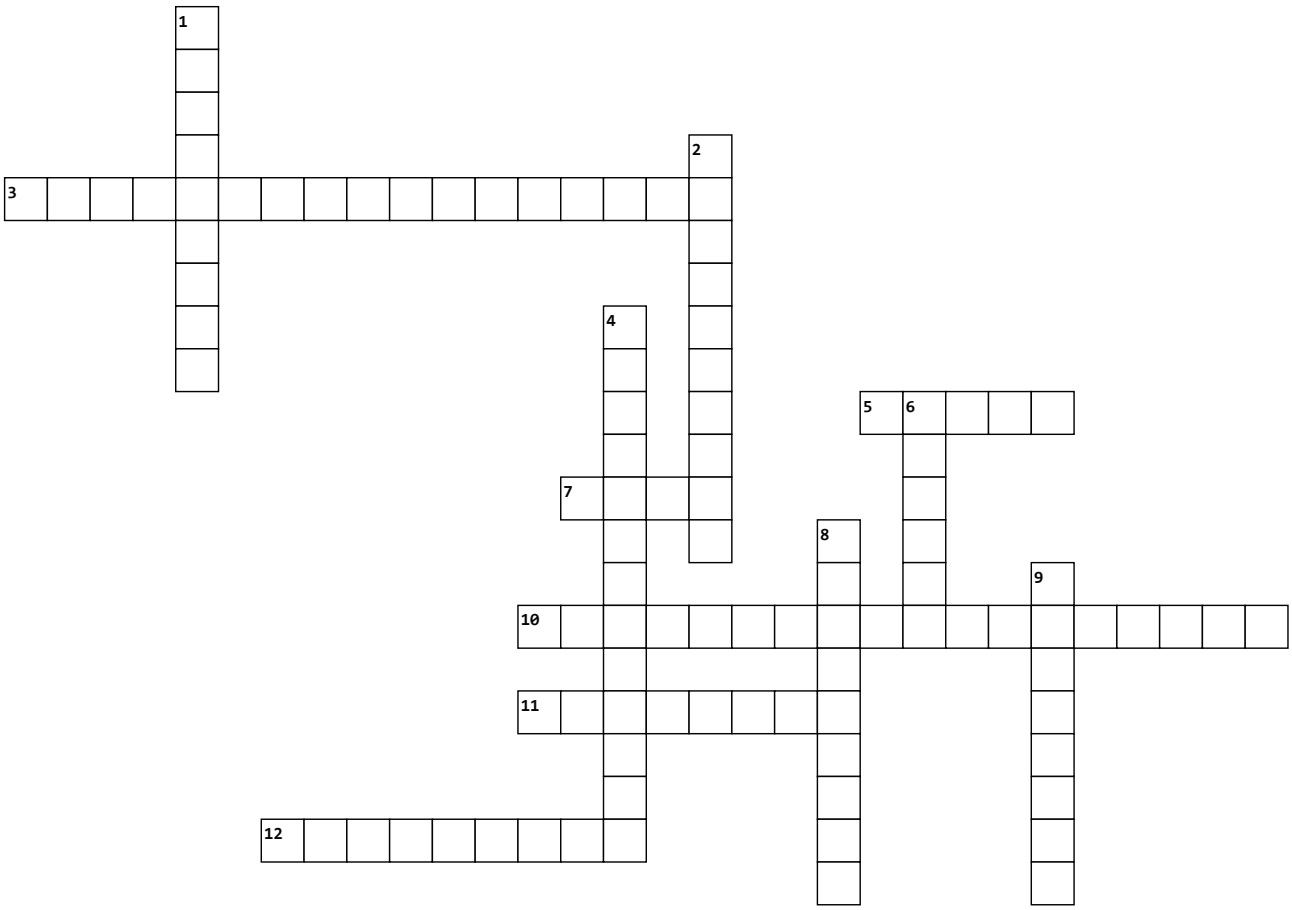
S. No	Date	Events
1	01.09.2022	**CME on "Genetic & Fetal medicine in obstetric practice" by General & Fetal Medicine sub-committee**
2	03.09.2022	CME on Endometrial Cancer- less by AOGD Oncology sub-committee
3	04.09.2022	CME on Infertility by DGF & AOGD (Physical)
4	10.09.2022	CME on Endometrial Cancer- less is more by AOGD Oncology sub-committee
5	19.09.2022	PG forum on Pregnancy with Anaemia
6	29.09.2022	Webinar by Endoscopy sub-committee
7	30.09.2022	AOGD Monthly clinical meeting at DDU Hospital

Forthcoming Events

S. No.	Date	Events
	06.10.2022	Webinar "Paradigm Shift in management of Ectopic Pregnancy" by Endoscopy Sub-committee
	07.10.2022	CME by Infertility sub-committee
	08.10.2022	Physical CME on RPL by Multidisciplinary sub-committee
	12.10.2022	Prevention of Thalassemia & Hemoglobinopathies by AOGD Genetic & Fetal Medicine sub-committee & State Blood Cell, Delhi
	15.10.2022	Physical event on AUB by Bayers medics
	17.10.2022	PG forum on Postmenopausal bleeding
	22.10.2022	Webinar by Oncology sub-committee
	27.10.2022	Webinar" by Endoscopy sub-committee
	28.10.2022	AOGD Monthly clinical meeting at ESI Hospital

Cross Word Puzzle

Nalini Bala Pandey*, Akansha Pandey**
*Consultant, **Senior Resident, Department of Obstetrics & Gynaecology, Maulana Azad Medical College, Delhi



Across

3. Chemical composition of Monsel's solution

5. How many consecutive cytology reports are required to be negative to discontinue screening for cervical cancer?

7. The recommended age to start HPV vaccination.

10. The area between the old and the new squamocolumnar junction on the cervix is called?

11. Cervical cytology smears are reported using which system?

12. While collecting the LBC sample, the cytology brush is rotated in which direction?

Down

1. The container in which the pap smear sample is collected.

2. Which grading system is used for classifying cervical lesions as CIN 1-3 as per colposcopy findings?

4. The most commonly used high-risk HPV DNA testing method is based on which genome testing?

6. Delphi screener and Evalyn brush are devices for self-sampling of which test?

8. Recently approved nonavalent HPV vaccine is named.

9. Upper age limit for single dose HPV vaccine is _____years.

Mail the answers to aogdeditor22@gmail.com. The correct answers and names of the three winners will be announced in the next issue.

AOGD Sub-Committee Chairpersons 2022-2024

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Breast and Cervical Cancer Awareness, Screening & Prevention Sub-Committee	Dr Mrinalini Mani	9811835888	drmrinal5@gmail.com
Infertility Sub-Committee	Dr Manju Khemani	9810611598	dr.manjukhemani@gmail.com
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Multidisciplinary Sub- Committee	Dr Kiran Guleria	9811142329	kiranguleria@yahoo.co.in

AOGD Sub-Committee Chairpersons 2021-2023

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Fetal Medicine & Genetics Sub-Committee	Dr Seema Thakur, Chairperson	9818387430	Seematranjan@gmail.com
	Dr Sangeeta Gupta, Co- Chairperson	9968604349	drsangeetamamc@gmail.com
Endoscopy Sub-Committee	Dr Kanika Jain	9811022255	dr.kanika@gmail.com

Proceedings ot the AOGD monthly clinical meeting at Deendayal Upadhyay Hospital on 30.09.2022

Urinoma in Pregnancy: An Enigma

Pinkee Saxena, Richa Madan, Urvashi, Soma Mitra, Sunita Seth, N Bindal, Monika Suri

Urinoma is as an encapsulated collection of urine outside the urinary tract as a result of disruption of the collecting system. Little is known about maternal urinoma during pregnancy.

Case: A 25 years old female, G3P1L0A1 with history of previous LSCS, presented to DDU hospital at 25 weeks of gestation with complaints of abdominal pain and decreased fetal movements. Her level II ultrasound showed a 22 weeks fetus along with a 19 x16x11 cm cyst in the abdomen on the left adnexa suggestive of left ovarian cystadenoma.

On admission, her vitals were stable. On abdominal examination, apart from a 24-26 weeks uterus, a 15 x 12 cm mobile, non-tender swelling was felt per abdomen which was separate from the uterus. Her blood investigations were within normal limits except for a deranged LFT. Urine routine and microscopy was full of pus cells. MRI done showed a thick walled multiloculated left adnexal cystic lesion measuring 27x17x 24 cm suggestive of giant serous cystadenoma.

Patient underwent an emergency laparotomy in view of acute abdomen. Intraoperative a large mass of approximately 25x20 cm was seen arising from retroperitoneum. Fluid was aspirated from the mass and sent for analysis which showed high levels of urea and creatinine. A provisional diagnosis of Urinoma was made. A PCN and PCD was inserted. Patient delivered at 36 weeks by LSCS. She is currently under follow up.

Discussion : Urinoma is an acute complication that occurs following an injury to the kidney or upper urinary tract. Diagnosis of this condition depends primarily on imaging studies. Conservative treatment is done for small urinoma. In large urinoma, urinary diversion is recommended.

Undiagnosed case of caesarean PPH

Sunita Seth, Usha Yadav, Shashi L. Kabra, Pratibha Nanda, Neeta Bindal

Placenta accreta spectrum (PAS) is an umbrella term for a variety of pregnancy complications due to abnormal placental implantation, including placenta accreta, placenta increta and placenta percreta.

Case: A 28 year old female patient , G2P1L1 35 weeks with previous LSCS who underwent LSCS in a private hospital in Ghaziabad in view of APH was referred DDUH.

On admission she was in shock, with BP 80/40 mmHg, pulse 120/min. On per abdomen examination uterus was contracted corresponding to 26wks. On per vagnium examination there was a vaginal pack which was soaked with blood.

She was stabilised, started on Noradrenaline and shifted to emergency OT with blood and blood products. In OT, on removing the vaginal pack profuse bleeding was seen. An immediate decision for laparotomy was taken. Intraoperative uterus was flabby with 700 ml of haemoperitoneum. Bladder was densely adherent to the uterus. Placental bits were found to be adherent to the uterine bed. Large vessels were seen invading the bladder. Above findings were suggestive of placenta percreta.

Obstetric hystrectomy with internal iliac ligation was done. As adequate haemostasis could not be achieved abdomen was packed and patient was shifted to ICU with pack in situ. Relaparotomy was done to remove the packs after 48 hrs. Further post operative period was uneventful and patient was discharged on day 10.

PAS is a potentially life threatening condition and should be managed surgically. Timely referral and a multidisciplinary team along with an ICU set up and blood bank facility is imperative for successful management of such cases.

Post MTP pain - A Diagnostic dilemma

Harvinder Kaur, Soma Kumari, Pinkee Saxena, Monika Suri

Pain post MTP always remains a diagnostic dilemma. Two cases are presented to highlight it.

Case1: A 26 year old female, P1L1A1 came to casualty with complaint of pain abdomen, vomiting and abdominal distension since last two days. She had history of MTP done at a private hospital four days back at 7 weeks of gestation. She also gave history of on and off fever since the last 10 days. She was tachypnoeic and in shock. Her pulse was 120/min, BP was 80/50 mm of Hg and was started on noradrenaline support. On abdominal examination , abdomen was distended with generalised tenderness, guarding and rigidity. Bowel sounds were absent. On per vaginum examination os was closed with bilateral forniceal tenderness. Exact size of uterus could not be assessed. Her investigations sent were normal. Ultrasound done showed a normal uterus with moderate ascites. In view of history of MTP with features suggestive of perforation peritonitis decision of exploratory laparotomy was taken. Intra operative uterus was found to be intact without any evidence of perforation. Bilateral tubes and ovaries were normal. 1400 cc of bilious fluid with pus flakes was present intra abdomen. An ileal perforation of 7x7 mm was seen 5 cm proximal to the ileocaecal junction. Rest of the organs were normal. Primary repair of the ileal perforation with diversion loop ileostomy was done. However the patient expired in ICU 6 hours after the surgery. The biopsy from perforation site showed acute on chronic inflammation with no granulation suggestive of typhoid perforation.

Case 2 : A 22 year old female, P1L1A1 was referred from a private hospital with suspicion of uterine perforation with bowel injury post MTP of 6 weeks gestation. She had complaint of mild pain in abdomen. On examination she had tachycardia and rest of the examination was normal. Ultrasound showed uterus bulky with minimal heteroechoic content in endometrial cavity, mild fluid in POD. Exploratory laparotomy was done which showed 1x2 cm perforation on the anterior aspect of uterus through which 3 inch of unhealthy omentum had gone inside the uterus. Serosal injury was seen in ileum. The uterine perforation was repaired and D&E completed under supervision. Patient was discharged on day 5 of surgery.

Discussion – These two case highlights the diagnostic dilemmas one faces post MTP. In such case other causes of pain in abdomen should always be kept in mind. Detailed past history is important and should be elicited. Weightage should be given to the opinion of primary provider . When in doubt, a CT scan or diagnostic laparoscopy or laparotomy should to done for a favourable patient outcome.

Events held under Aegis of AOGD in September 2022

DHEERA Award by FOGSI President

Dr. Asmita Rathore
Dr. Abha Singh
Dr. Neerja Bhatla
Dr. J B Sharma
Dr. Ashok Kumar
Dr. Richa Sharma

FOGSI Individual Awards & Prizes -2022

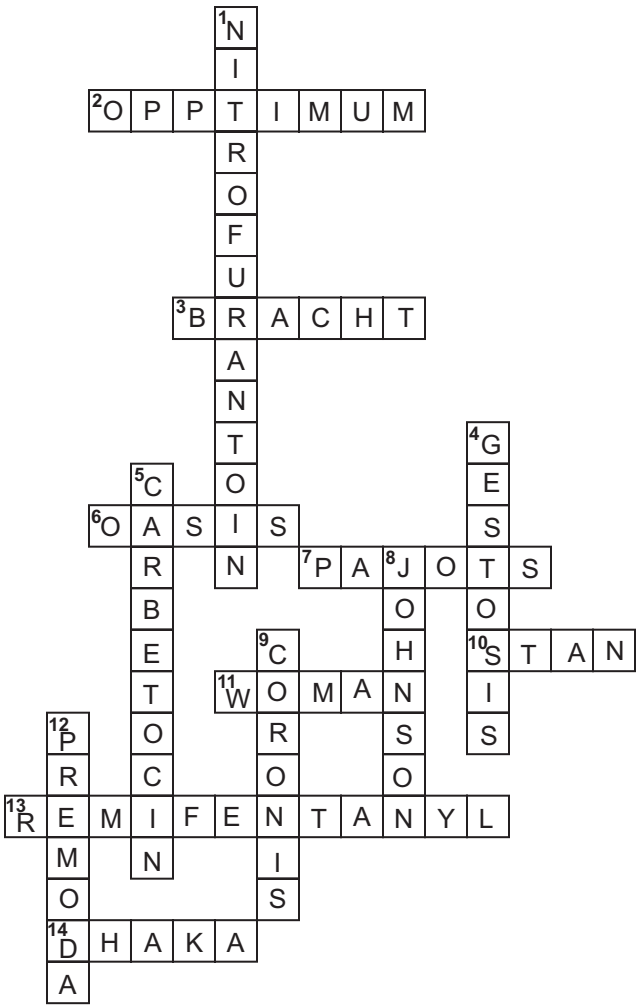
Award	Name
FOGSI-Dr. R D Pandit Research Prize 2022	Dr. Kritika Agnihotri
FOGSI-Dr. Kumud P Tamaskar Prize 2022	Dr. Anjali Chaudhary
FOGSI-Dr. Kamini A. Rao orator for North Zone	Dr. Neha Varun
FOGSI Corion awards 2022	Winner: Dr. Manju Puri 1st Runner up: Dr. Richa Sharma (Senior) 1st Runner up: Dr. Raj Laxmi Mundhra (Junior)
FOGSI-Dr. Nimish R. Shelat Research Award 2022	Dr Divya Pandey
FOGSI-Dr. Shanti Yadav Award in Infertility 2022	Dr. Swetha Sri
FOGSI - Dr. Rajat Ray Award in Fetal Medicine 2022	Dr Divya Pandey
Best paper published in FOGSI Journal during the year 2021 in Junior Category	Dr. Nikita Kumari (Second Prize) Dr. Zeba Khanam (Third Prize)

CME on "Genetic & Fetal medicine in Obstetric practice" on 1st September
Gen & Fetal medicine Subcommittee

CME on Endometrial Cancer- less is more on 10th September
AOGD Oncology Sub-committee

CME on Infertility on 4th September
DGF and AOGD

Answer key of Quiz of September 2022



Winners of the monthly quiz, September Issue 2022

1. Dr Lekshmi S A
2. Dr Anuradha Sharma
3. Vijayata Thakur

Association of Obstetricians & Gynaecologists of Delhi

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