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# AOGD BULLETIN

Volume 21 I October 2021 I Monthly Issue 6


***Dedicated Issue:***

***"Gynaecological Malignancies"***


**AOGD SECRETARIAT**

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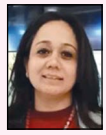

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# Foreword

Warm greetings for the upcoming festive season to all!

It gives me immense pleasure in presenting this issue of AOGD bulletin on **Gynaecological Malignancies**. The period of intense restrictions and lockdown has been most difficult for patients with malignancies due to health care services being primarily diverted to COVID care. With the number of COVID cases finally coming to a controllable count, our life seems to be going back to normal now and a sense of relief for these patients as well. This month's issue is also based on theme of the year 2021-22, **"Promoting Women's Health by Strong Will and Quality Skill"**. The issue is highlighting the recent advances in the vast world of prevention and management of Gynaecological Malignancies.

Gynaecological Malignancies have always been an enigma for practicing doctors with unpredictable outcomes. This issue is focusing on important topics of Gynae cancers like Premalignant Lesions of Vulva, Cervical Cancer Elimination 2030: Role of a Gynaecologist, Recent Advances in management of endometrial cancer, Update on Management of Molar Pregnancy, Approach to an Adnexal Mass, and Genetic Testing in Gynaecological Cancers. The amalgam of topics is like visiting the old and new worlds together and I am sure it would be a delight for the readers.

I would like to congratulate the committee members and editorial board for putting forward this fantastic line up and wish them luck for future. Despite the difficult times the learning process must go on and AOGD has been most forthcoming in being the source of knowledge to both old and new generation of doctors. Wide variety of information through webinars and e-CMEs with most recent updates on various topics have been provided through virtual platforms and has been a delight to attend. I wish all the best to AOGD forum for bringing out the best of e-learning in time ahead as well.

Keep up the good work!

S. Batra.

**Dr Swaraj Batra**
Advisor AOGD

# From the President's Pen

Greetings to All AOGDians!

October brings us the holy festival of Navratri. It is a celebration of feminity, strength, determination, warmth, courage and all the beautiful things that makes a woman. With the celebration of Navratras, get geared up for our academic festival which is going to take place on 19th- 21st November 2021. All our AOGD members will surely get the flavor of well-crafted and designed virtual, unique academic activities.

The theme of this bulletin on "**Gynaecological Malignancies**" will help all Gynaecologists to help women fight all odds against cancer. The incidence of Gynecological cancers is increasing in India and there is wide disparity in diagnosis and treatment of malignancies in our country owing to lack of awareness, apathy, geographical and financial constraints. There is not only a need for upgrading awareness, life style and access to health care but also a need to update the knowledge of Gynaecologists to the changing concepts in diagnosis and management. There are important articles in this issue especially Role of Gynaecologists in Cervical Cancer Elimination by 2030, Recent Advances in Management of Endometrial Cancer, Genetic Testing in Gynaecological Cancer and many more which will surely guide you all for better prevention and management of Gynaecological cancers. Our enthusiastic editorial board has compiled this bulletin very well so as to benefit everyone.

***"Persistence and resilience only come from having been given the chance to work though difficult problems." – Gever Tulley***

**Dr Achla Batra**
President, AOGD (2021-2022)


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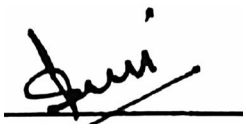
# From the Vice-President's Pen

Dear Members

Warm wishes and greetings to all of you. This beautiful month of October ushers in the festive season and is also the harbinger of the much-awaited winters ahead. Another important relevance of this month is that it is celebrated as the Breast Cancer Awareness Month. To commemorate this, our Editorial Team brings forth for all of you an update on Gynaecological Malignancies. The topics are very practical and well selected and will definitely help us all in our daily practice.

The preparations for our 43rd Annual Conference are now at their dizzy peak. We hope all of you have registered for this most exciting scientific event of the year with a multitude of Workshops, Key notes and Orations as well as quiz, paper and posters for our young members. Waiting eagerly to see you all.

Wishing you all a very Happy Dussehra and Diwali. Enjoy the festivities safely.



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Hands-on Practical Workshop (3 hours)
on **"Obstetrics Critical Care"** from October 2021.
Interested candidates to contact
**Ms Sarita,** AOGD Office: Mobile No- 9211656757

# From the Secretary's Desk

Warm greetings to all !

Amidst the wonderful festive season, we bring before you another interesting and dedicated issue of AOGD bulletin full of academics and important information for our AOGD members.

We are all set for our **43rd Annual AOGD Conference** from **19th-21st November.** We request all our members to participate in this academic bonanza which will be filled with wonderful thought provoking scientific sessions presented by state, national and international faculty. There are dedicated 12 pre and post congress workshops which will add flavour to the main conference. There has been a tremendous response for the competition and free papers and posters from our young and experienced AOGD members both. We have even worked out a simple online portal for conference registration and AOGD membership for convenience of all. Above all, we are having a 'Talent Hunt' contest to showcase the extra-curricular potential of our AOGD members. So, inviting you all once again to be part of all academics and fun during this most awaited annual event of Delhi.

As regards this month's bulletin, I congratulate the editorial team for yet another interesting and useful issue on **"Gynaecological Malignancies".** It aptly covers all the important aspects viz. Premalignant lesions of vulva, recent advances in management of endometrial cancer, molar pregnancy and adnexal masses. An interesting aspect of genetic counselling in gynaecological cancers and vision for 2030 for cervical cancer elimination has also been added.

I am sure these evidence based articles with practical tips and recent advances in field of gynaecological oncology will be thoroughly useful for our readers.

Happy reading,

**Dr Monika Gupta**
Secretary, AOGD (2021-2022)

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# From the Editor's Desk

Greetings from the editorial team!

We wish you all a happy and prosperous festival season and welcome you to the sixth issue of AOGD monthly bulletin dedicated to "**Gynaecological Malignancies**".

We are thankful to Dr Swaraj Batra, Advisor AOGD for sparing her valuable time to write foreword for this issue. We are also grateful to Dr Saritha Shamsunder, former president ISCCP for choosing topics that will help in updating our readers on recent developments in Gynaecological cancers. We also appreciate the hard work put in by all the authors in preparing the articles.

In recent years, incidence of Vulval Intraepithelial Neoplasia has increased by four folds. Early diagnosis and treatment of **Premalignant Lesions of Vulva** is crucial to bring down the morbidity and mortality associated with vulval cancers. Among all Gynaecological malignancies, cervical cancer is the only malignancy that can be prevented by vaccination and timely management of premalignant lesions detected during routine screening. Despite the preventive and screening measures available for a long time, cervical cancer is still the fourth most common cancer among women and is responsible for significant mortality worldwide. Due to the cost effective measures available, WHO has set 90-70-90 targets to be achieved for **Elimination of Cervical Cancer by 2030**. Treatment and follow up of the Molar pregnancy is important for early diagnosis of Gestational Trophoblastic Neoplasias. **Update on Management of Molar Pregnancy** highlights the protocol to minimize acute complications and timely diagnose GTN. The article on **Recent Advances in Management of Endometrial Cancer** focuses on evolving therapeutic modalities based on the Molecular classification. Management of adnexal mass can be challenging but a systematic **Approach to an Adnexal Mass** can avoid unnecessary surgical interventions and possibility of missing malignancy. **Genetic Counselling in Gynaecological Cancers** is important for women with family history of malignancy.

We hope the information provided in this issue will help the readers in their clinical practice.

Happy reading!

**Dr Rekha Bharti**
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# Premalignant Lesions of Vulva

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## Introduction

Premalignant conditions of the vulva are changes to vulvar cells that make them more likely to develop into cancer. These conditions are not yet cancer. But if they aren't treated, there is a chance that these abnormal changes may become vulvar cancer. A number of premalignant conditions affect vulva including vulvar intraepithelial neoplasia (VIN), vulvar Paget's disease, and lichen sclerosis. The most challenging part for clinician is to differentiate between normal variants, benign lesions, and potentially serious lesions.

Incidence of VIN has increased fourfold and has now become a common problem particularly among women in their 40's in whom there is a strong association of HPV infection, while the incidence of vulvar cancer remains constant.

## Historical Classification of Premalignant Lesions of Vulva

Earliest classification was done in 1965 by Kaufman and Gardner where they grouped premalignant vulvar lesions into three groups- erythroplasia of Queyrat, Bowen's disease and carcinoma simplex.

In 1976 the International Society for the Study of Vulvar Disease (ISVVD) used the terms mild dysplasia (VIN 1), moderate dysplasia (VIN 2) and severe dysplasia (VIN 3).

In 2004 the ISVVD replaced it with a single grade classification system in which only high-grade disease was classified as VIN. It was further classified as HPV-positive usual-type VIN (formerly VIN 2/3) or HPV-negative differentiated VIN (dVIN)/simplex-type carcinoma in situ (CIS).

## Current 2014 WHO Classification/ ASCCP/ISVVD 2015 Classification

In order to unify the classification of HPV associated squamous lesions of lower genital tract, term Vulvar Intraepithelial Neoplasia (VIN) was replaced with Vulvar Squamous Intraepithelial Lesions (SIL). Vulvar lesions were reclassified by ISVVD in 2015, as Low Grade Squamous Intraepithelial Lesions of Vulva (vulvar LSIL) and high grade squamous intraepithelial lesion of vulva (vulvar HSIL), dVIN remained the same.[1] A similar classification was proposed by WHO and adopted by ASCCP.

LSIL includes flat lesions associated with basal atypia and koilocytic changes (formerly known as VIN1). HSIL includes usual type VIN (uVIN, previously referred to as VIN 2 and VIN 3).

Other intraepithelial vulvar lesions like paget's and melanoma in situ are rare.

## Etiopathogenesis

**Table 1:** 2015 International Society for the Study of Vulvovaginal Disease Terminology of Vulvar Squamous Intraepithelial Lesions and 2004 Terminology <=

| 2015 Terminology | 2004 Terminology |
|---|---|
| Low-grade squamous intraepithelial lesion of the vulva (vulvar LSIL, flat condyloma, or HPV effect) | Condyloma, HPV effect* |
| High-grade squamous intraepithelial lesion of the vulvar (vulvar HSIL, VIN usual type) | Usual-type VIN (subdivided):<br>a. VIN, warty type<br>b. VIN, basaloid type<br>c. VIN, mixed (warty or basaloid) type |
| Differentiated type VIN | Differentiated type VIN |

Abbreviations: HPV, human papillomavirus; VIN, vulvar intraepithelial neoplasia.

*Sideri M, Jones RW, Wilkinson EJ, Preti M, Heller DS, Scurry J, et al. Squamous vulvar intraepithelial neoplasia: 2004 modified terminology, ISSVD Vulvar Oncology Subcommittee. J Reprod Med 2005;50:807-10.

Data from Bornstein J, Bogliatto F, Haefner HK, et al. The 2015 International Society for the Study of Vulvovaginal Disease (ISSVD) Terminology of Vulvar Squamous Intraepithelial Lesions. Obstet Gynecol 2016:127(2):264-8.

High grade squamous intraepithelial lesion (HSIL/ Usual type VIN) is commonly associated with carcinogenic genotype of HPV (16, 18, 31), while LSIL is often associated with low risk HPV subtypes (6, 11).[2]

The anogenital epithelium of lower genital tract including lower rectal mucosa has a similar embryonic origin and is thus susceptible to similar exogenous agent (HPV). SIL in this area can be multicentric and multifocal having synchronous

squamous neoplasia of other sites (cervix, vagina and anus). 60% of VIN/ VaIN (vaginal intraepithelial neoplasia) have persisting or synchronous CIN.

Other risk factors are cigarette smoking, immunocompromised state (HIV).

Differentiated VIN (dVIN) is usually HPV negative and associated with other vulvar dermatological conditions like lichen sclerosis and lichen planus. It is associated with more rapid progression to squamous cell carcinoma especially lichen sclerosis associated with dyskeratosis, parakeratosis and basal cellular atypia. Risk of vulvar squamous cell carcinoma in lichen sclerosis is 5%, earlier detection and aggressive management of lichen sclerosis can lead to reduction in development of SCC.

Premenopausal women are more likely to have HPV associated VIN, while dVIN affects mostly the post menopausal age group.

## Approach to a Case of Vulvar Lesion

*Clinical presentation:* Pruritus is the most common presentation. Some may have vulvar pain, burning or dysuria. In 40% patients, there are no symptoms but a vulvar lesion is noted either by the patient herself or during routine gynaecological examination. Persistent abnormal cervical cytology in the absence of any cervical abnormality can be due to vulvar pathology as lesions of LSIL are multicentric.

After a detailed history regarding symptoms, duration of symptoms, prior history of vulvar SIL, genital warts, cervical neoplasia, HPV vaccination status, smoking, HIV status a thorough physical examination should be performed noting the lesion location, colour, characteristic, ulceration, and cervix status.

*Examination:* There is no pathognomonic clinical appearance but most of the vulvar SIL lesions are raised and white multifocal lesions, located on non hairy vulvar part mainly the interlabial grooves, posterior fourchette, and perineum. Colour can even be red, pink, grey or brown and macular lesions are sometimes noted. Many a times more than one pattern can be seen in same patient.

It is difficult to differentiate between genital warts (condyloma acuminata) and LSIL. More worrisome is the fact that it may be difficult to differentiate between high grade SIL, dVIN, invasive vulvar squamous carcinoma as anyone of them can present as a plaque, ulcer or a mass (warty, nodular, fleshy) and can even coexist in the same patient. Colposcopy and biopsy of lesion is further required for the proper management.

*Vulvoscopy:* It is performed when there is visible vulvar lesion or if there is persistent abnormal cytology report in the absence of cervical pathology or in cases of focal vulvar symptoms like itching, burning or dysuria without any clear etiology. It is done in a similar manner to cervical colposcopy. 3-5% acetic acid is applied to external genitalia and observed for 3 to 5 minutes for the solution to act on the cells and for the lesion to appear white, followed by biopsy of lesion. Lesions can be well delineated on application of Toludine blue on vulvoscopy. Multizonal disease should always be suspected and examination of perianal area, vaginoscopy and colposcopy should always be done along with vulvoscopy.

*Vulvar biopsy:* Depending on the lesion, either punch biopsy (removing 3-5 mm circular skin piece with all skin layers) or excisional biopsy (removing of entire lesion possible) is performed. A pigmented lesion and ulcerative lesions less than 1cm should be completely excised, for a large ulcerative lesion incisional biopsy is taken with a bit of normal looking skin. Hemostasis can be achieved by either silver nitrate sticks, electro cautery or by taking sutures.

## Histopathology

*Vulvar low-grade SIL (LSIL)*– is characterized by cytologic atypia in the upper two-thirds of the epithelium.

*HSIL*- is characterized by loss of maturation of the middle (VIN 2) and upper third to full thickness (VIN 3) of the squamous epithelium. It can be warty or basaloid or a mixture of both.

*dVIN*- epithelium is thickened and parakeratotic with elongated and anastomosing rete ridges confined to the parabasal and basal portion of the rete pegs having minimal/no atypia above the basal or parabasal layers. p53 is frequently abnormally expressed (either overexpressed, no expression at all).

## Prevention of Vulvar SIL and HPV Associated Carcinomas

The quadrivalent (active against HPV subtypes 6,11,16,18) and 9-valent HPV vaccines (6,11,16,18,31,33,45,52,58) decreases the risk of vulvar SIL. Based on immunogenicity, studies

have shown that the 9-valent HPV vaccine, has the potential to prevent up to 90 percent of HPV-associated vulvar carcinomas.

## Treatment

*LSIL*: They are not premalignant lesions. It is mostly self limiting and resolve within a year or two. They do not require treatment unless symptomatic.

*HSIL:* These are precancerous lesion, associated with 20% squamous cell carcinoma of vulva, thereby requiring definite treatment. Focus of the treatment is to alleviate symptoms as well as to prevent progression to vulvar carcinoma while preserving vulvar function and anatomy as much as possible. Treatment modalities include– excision, ablation and topical treatment.

***Excision:* Indications include**

1. Single lesions (complete removal is possible, providing both diagnostic specimen and treatment simultaneously)
2. When there is high possibility of invasive disease (ulcerative lesions with irregular margins)
3. Significant high risk factors (previous treated vulvar HSIL, dVIN, Lichen sclerosis, immunosuppression)
4. dVIN

***Type of excision***

Wide local excision is most preferred method, removing lesion with additional *1cm margin*. Epidermis is removed along with little amount of dermis which helps to rule out early invasive cancer. Recurrence is common, if visible lesions seen then treatment is required. In case of microscopic positive margins but no gross visible lesion, close follow up is done. Being a multifocal disease, excision at one site does not reduces the risk of lesions at any other site on vulva.

*Simple/total vulvectomy*: Removing entire vulva with perineal tissue and some subcutaneous tissue

*Skinning vulvectomy:* In this vulvectomy subcutaneous tissue is preserved. Skin grafting can be done along with procedure.

*Ablation*: is done in cases of multifocal lesions and lesions involving clitoris, urethra, vaginal introitus or anus. Biopsy is must before performing ablative procedures to rule out invasive cancer. $CO_2$ laser most frequently used, others are argon laser and ultrasonic surgical aspiration. Depth of tissue destruction depends on area of concern (1 mm for hair free epithelium, 3 mm for hairy areas of vulva)

*Topical Treatment:* can be done for clitoral lesions in women who prefer to avoid excision/ ablation. It requires long term compliance. Invasive carcinoma needs to be ruled out first. **Imiquimod** is applied on individual lesion for 3-5 times a week for 4 months. Side effects include inflammation and erythema. **Fluorouracil** is not used widely due to unwanted side effects like burning, edema, and painful ulcerations. It causes chemical desquamation of HSIL, used as a last resort. **Cidofovir** gels are under controlled trials and have shown similar efficacy to imiquimod.

Even with complete treatment, approximately one-third of patients develop recurrent vulvar SIL.[3] The risk of recurrence with progression to invasive carcinoma is approximately 8%. Therefore, a close long-term surveillance of the entire lower genital tract is required. Follow-up is done every six months for five years after the last treatment and then annually.

## Paget's Disease

Vulvar extramammary Paget's disease (EMPD) is a rare non-squamous intraepithelial lesion of the vulva. It occurs mainly in postmenopausal women (median age of 72 years). The most common signs and symptoms are itching, burning and post menopausal bleeding. It is usually multifocal, with multiple extensive lesions in form of well demarcated scales and erythematous-white plaques. It has the potential for dermal invasion and there is positive association with an underlying adenocarcinoma of breast, pancreas, endometrium, bladder, stomach and rectum.[4]

Treatment is wide local excision upto the depth of 4–6 mm to include the pilosebaceous units and skin adnexal structures. In cases of underlying adnexal adenocarcinoma or stromal invasion of EMPD over 1 mm, aggressive treatment is required with excision to the fascia in the involved area, and bilaterally inguinofemoral lymphadenectomy. Vulvoperineal reconstruction can be done by skin or muscle flaps. Radiation therapy is done in selected cases only.

Overexpression of the HER-2/neu protein has been seen in about 30% of vulvar EMPD cases. They have more aggressive behaviour and higher recurrence rate. In such cases targeted therapy with trastuzumab have shown good results. Treatment can result in a significant regression of disease and resolution of symptoms

No correlation has been found between disease recurrence and margin status, recurrence is common specially disease involving the perineum. Long-term monitoring is recommended as recurrence can be noted many years after the initial treatment and repeat surgical excision is often necessary.

## Lichen Sclerosis

It is one of the most common vulval disorders seen in Gynaecology clinics. It is a benign, chronic and progressive condition affecting any age group but more common in perimenopausal/ postmenopausal and prepubertal girls. Etiology is unknown, though studies have shown genetic association, autoimmune theory (LS is associated with autoimmune disorders like vitiligo, alopecia areata, thyroid disorders, pernicious anaemia, diabetes mellitus), hormonal theory (common in low estrogenic states), associated infections.[5]

Intense pruritus that interferes with sleep is the commonest symptom. Other symptoms are pain, anal discomfort, dyspareunia (due to shrinkage of introitus) and dysuria (due to fusion of labia minora over urethra in advanced cases). Sometimes women can be asymptomatic and lesion noted during routine Gynae check up.

On examination, white atrophic papules, plaques are seen mainly affecting labia minora and majora. Continous scratching can cause excoriation and thickened epidermis (lichenification). There can be yellow waxy appearance of vestibule with absence of fordyce spots (normal sebaceous glands on inner side of labia minora). In advanced cases, there is shrinkage of introitus with a pinhole orifice.

A punch biopsy can confirm the diagnosis, histopathological findings shows thinned out epidermis, mild epidermal acanthosis, upper dermis homogenization and lymphocytes below it. **Differential diagnosis** includes lichen planus (vagina is involved in lichen planus and spared in lichen sclerosis), lichen simplex chronicus, contact dermatitis, atopic dermatitis, vitiligo, candidiasis and psoriasis (lesions are red rather than white).

## Management

Lichen sclerosis is associated with increased risk to develop squamous cell carcinoma. Both can coexist in same woman. dVIN which is a precursor of SCC is associated with lichen sclerosis. Early treatment of all cases is required as it not only relieves symptoms but also reverses many skin changes. Topical corticosteroids are the mainstay of treatment. Topical clobetasol propionate, a potent corticosteroid is most commonly used. Thickened plaques respond less to topical treatment and requires triamcinolone injections.

Other second line drugs are tacrolimus, oral acitretin, topical testosterone, UVa1 phototherapy, and photodynamic therapy. Recently PRP and mesenchymal stem cell therapy have shown promising results. Vulvoperineoplasty is required in advanced cases of scarring and introitus narrowing. Due to chronic nature of disease and progression to SCC, long term follow up is required.

## Conclusion

There are no specific screening programs to detect vulvar carcinoma or its precursor lesions, and therefore gynaecologists should be aware of the clinical presentation, behaviour and management of the different existing premalignant vulvar lesions.

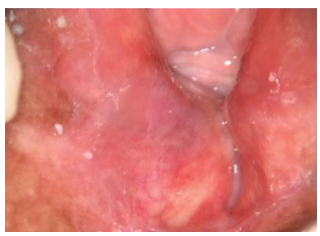

**Fig 1:** VIN lesions on Vulvoscopy on application of acetic acid

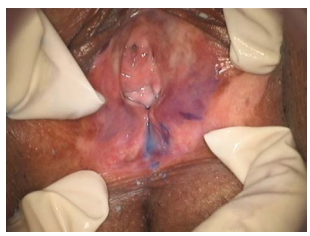

**Fig 2:** VIN on Vulvoscopy on Toludine blue application

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# Cervical Cancer Elimination 2030: Role of a Gynaecologist

**Jyoti Meena[1], Neerja Bhatla[2]**
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## Introduction

Cancer of the uterine cervix is the fourth most common cancer among women with an incidence of 604,127 cases and 341,831 deaths reported globally in 2020, vast majority of which occurs in low-and-middle-income countries.[1] Cervical cancer is a curable disease with a well-established long pre-cancerous phase and can be effectively prevented through screening and treatment of pre-cancerous lesions. In addition, if detected in its early stages and promptly treated more than 90% of lesions can be cured.[2] Therefore, HPV vaccination and cervical cancer screening and treatment form part of WHO guidance to countries. Despite these cost-effective interventions, the global disparities in infrastructure and resources required in cervical cancer treatment remains extreme both across and within countries.

To achieve cervical cancer elimination bold strategic actions are needed: improving community awareness; expanding workforce capacity; strengthening healthcare systems; accelerate the introduction of affordable technology into screening and treatment algorithms; nationally scale organized, population-based prevention and treatment platforms. To ensure optimal effectiveness, the strategic actions must be developed in concert with healthcare policy makers and providers and the women themselves.

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 August 2020, the World Health Assembly passed a resolution calling for elimination of cervical cancer and adopting a strategy to make it happen and officially launched the global strategy for cervical cancer elimination on 17th November 2020.

## Principles and Elimination Goal

"Elimination of a public health problem" is defined as achieving the measurable global targets set by the World Health Organization for a specific disease, based on population data. 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
- Screening: 70% of women screened using a high-performance test by the age of 35, and again by the age of 45
- Treatment: 90% of women identified to have cervical disease treated including
  - 90% women with pre-cancer treated
  - 90% of women with invasive cancer managed

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

## Why the 90-70-90 Targets are Key to Success

Interventions to meet the three targets must be implemented simultaneously and at scale for maximum impact. Implementing all three pillars of the strategy will contribute to the immediate and accelerated reduction in mortality rates that result from the treatment of invasive cervical cancers; the decreased incidence rates as a result of wide-scale implementation of screening and treatment services and by vaccination against HPV which offers protection against cervical cancer for girls.[4] With this WHO triple-intervention strategy it is projected that it will result in 33.9% reduction in mortality rate by 2030 and 96.2% by 2070, which will help in saving more than 62 million women's lives by 2120.[5]

But achieving these targets will only be possible through the adoption of national programmes delivered by health services that address the personal, cultural, social, structural and economic barriers that currently hinder access by women and girls.

1. **90% target: Role of HPV vaccination**

Vaccination of adolescent girls is the most effective long-term intervention for reducing the risk of developing cervical cancer. WHO recommends two-dose vaccination schedule for young adolescent girls between 9 and 14 years of age.[6] The long-term benefit of HPV vaccination makes it important to initiate and sustain this approach in all countries. However, HPV vaccine coverage is inequitably distributed across the countries in the world with high income countries achieving higher vaccine coverage. 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. High cost and short supply have significantly constrained the ability of many countries to introduce HPV vaccine into national immunization programme (NIP). Therefore, Strategic advisory group of experts on immunization (SAGE) in 2019 recommended flexibility in timing between two doses with an extended interval for administration of the second dose up to 3-5 years after the first dose for younger girls aged 9 or 10 years if needed.[7] Currently, new prophylactic HPV vaccines are being analyzed for their safety and efficacy. A bivalent Chinese HPV vaccine has been licensed and an indigenous Indian qHPV vaccine has successfully completed the phase III trial for females and males aged 9–26 years. Other trials are also ongoing to address the possibility of a single-dose vaccine. Reduced number of doses, increasing the flexibility of intervals and fixing the vaccination schedule as per age-group would be cost-saving, and would also help in facilitating delivery thus, improving acceptance and enhancing vaccine coverage.

2. **70% target: Role of screening**

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, pathology), and disease management. In LMICs cytology-based programmes have been difficult to implement, and where they have been implemented screening coverage is low. Visual inspection of the cervix with acetic acid (VIA), followed by treatment (screen and treat), is an alternative approach to secondary prevention in resource-constrained settings.

HPV testing offers superior specificity and its strong negative predictive value means women who test negative only need to be re-tested after a minimum interval of five years. Providing women with the option of self-sampling contributes to acceptability and facilitates access. The effectiveness of screening is determined not only by the accuracy of the screening test, but also by screening coverage and linkages to diagnostic and treatment services.

3. **90% target: Role of treatment of precancerous lesion and invasive cancer**

WHO recommends two approaches for screening and treatment: the screen-and-treat approach and the screen, triage and treat approach.[8] WHO recommends HPV DNA testing as the primary screening method for regular cervical cancer screening starting at the age of 30 years with regular screening every 5-10 years. However the existing programmes with quality-assured cytology/VIA as primary screening should be continued until HPV DNA testing is operational.

In screen and treat approach the decision to treat is based on a positive primary test alone without triage and if patient is eligible for ablative treatment, thermal ablation should be done if possible at the same visit and if not feasible can be done on next visit.

While in the screen, triage and treat approach, if primary screening test is positive triage test (partial genotyping, colposcopy, VIA or cytology) is done and decision to treat is made when both primary and triage test are positive with or without histologically confirmed diagnosis. If patient is not eligible for ablative treatment, excisional treatment can be done on same day with large-loop excision of the transformation zone (LLETZ). If facility is not available on site, women need to be referred for excisional procedure or further evaluation.

Timely assessment and referral of women with suspected or confirmed cervical cancer are crucial for saving lives and preventing disability. Comprehensive management of invasive cervical cancer requires well-equipped, appropriately

qualified health providers and access to surgical, radiotherapy and chemotherapy services. Management depends on the stage of the disease. Palliative care should be integrated into the treatment plan and provided throughout the course of the disease.

Strengthening the referral pathways and linking all levels of care will ensure timely management of patients. Treatment plan should include all aspects of care including pain management and providing end-of-life care along with psychosocial care and spiritual support for women as well as their families.

## Cervical Cancer Elimination: Role of a Gynaecologist

Gynaecologists cater to a huge population of female aged 9-45 years. In India there are approximately 59.7 million girls and 272.8 million women, who are eligible for cervical cancer vaccination and screening.[9] Gynaecologists see and treat patients with cervical cancer, hence know the damage caused to the women by this cancer and ultimately to her family. Besides this, patients have full trust in their care-provider and listen to their advice and look upto them to clear their doubts. They form a crucial link between population at risk for developing cervical cancer and higher treatment centers, thus there is ample scope for gynecologists in the drive for elimination of this public health problem.

## Opportunities for Counselling

Young girls and women visit Gynae OPD with various complaints and every visit gives an opportunity to the Gynaecologists to counsel them about cervical cancer and its prevention with vaccination and screening. Counselling for immunization and screening should be done routinely for all patients coming to OPD. Besides counselling a comprehensive prevention strategy must also include providing information on sexual and reproductive health, safe sexual practices like delaying sexual debut, decreasing number of sexual partners and use of condoms and educate the parents and girls to practice a healthy lifestyle which is critical for a healthier population for sustainable development.

## Counselling for Vaccination

Parents accompanying young girls who attend gynae OPD should be explained regarding cervical cancer, nature of this disease, HPV being the necessary cause for its causation and the availability of vaccines against this virus which can prevent development of cervical precancerous lesions and cancer. Gynecologist should use every opportunity to explain parents of young girls regarding efficacy and safety of the vaccines and why it is important to vaccinate young girls. Parents should be allowed to clarify their doubts and fears regarding any myths surrounding vaccination. It is important not to miss out counselling older girls and women regarding catch-up vaccination if not vaccinated during target age-group. Even women with history of prior cervical screening abnormality (abnormal pap/ positive HPV test) should also be given the option of vaccination. However, proper counselling should be done prior to vaccination informing that vaccine will not have any therapeutic effect on pre-existing HPV infection/associated disease and the potential benefit will not be same as in those vaccinated before their sexual debut.[10] Communication is the key to ensure successful and optimal vaccine coverage. It is very important to provide valid information concerning HPV vaccines especially by gynaecologists who provide vaccine through clinics or general practice. Address all concerns and queries related to vaccination and end with strong recommendation. Maintain strong doctor-patient relationship to help with challenging immunization conversation. One can give personal examples of how you choose to vaccinate children in your family and educate the parents and women using posters, videos and flyers to have an visual impact.

## Counselling for Screening and Treatment

Explain women about long precancerous phase of cervical cancer, which is amenable to screening and early detection. Educate them about the screening methods available, test procedure and the test outcomes. Inform them about the available treatment options in case of abnormal result and about the testing frequency and importance of getting screened at least twice in lifetime at 35 and 45 years. Even the option of self-sampling should be given to women especially those residing in difficult to reach areas, especially during COVID times, curtailing travel and physical contact.

Besides this single visit approach should be practiced wherever possible to minimise non- compliance and loss to follow up. VIA with thermal ablation, LLETZ or

cryotherapy can be performed in same sitting with prior pre-test counselling of the women. Explain her about post procedure follow-up and when to come for next visit. In case of suspicion for high grade lesions and invasive cancers, timely referral to higher cancer centers is of paramount importance.

## Counselling for Palliative Care

Palliative care is an essential element of cervical cancer control. In case of advanced disease- palliative care, psychosocial care and counselling helps improve the quality of life of patients and their families facing the problems associated with the illness. Palliative care is best provided using a multidisciplinary team approach. Gynaecologist must provide information and support to the patients and their family and should refer them to higher level facilities for palliative care and management of acute problems.

## Conclusion

Gynaecologists play a crucial role in imparting knowledge and creating awareness among the eligible women and girls for vaccination and screening. However, when counselling the older women emphasis should be given on importance of screening in this age group. Palliative care should be integrated into the treatment plan and psychosocial and emotional support should be provided to the women and their families.

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# Recent Advances in Management of Endometrial Cancer

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The incidence of endometrial cancer continues to be on rise with 75% increase in number of cancer cases and 300% increase in number of cancer deaths in the last three decades.

Type I carcinoma or endometrioid carcinomas comprise 80–90% of all sporadic cases of uterine corpus cancer. They are histologically adenocarcinomas, and often well-differentiated. They are estrogen-dependent, and are associated with obesity, estrogen-based hormone replacement therapy, nulliparity, estrogen-secreting tumors and polycystic ovarian syndrome. They may be associated with hyperlipidemia, hypertension, and diabetes mellitus. The rest 10-20% are type II carcinomas or non-endometrioid carcinomas, and include clear cell, mucinous, squamous, transitional cell, mesonephric, and undifferentiated carcinomas. They are primarily non estrogen-dependent and occur in older multiparous women with normal body mass index (BMI). Grade 3 endometrioid carcinomas may be considered Type II carcinomas.

**Table 1:** The International Federation of Gynecology and Obstetrics (FIGO) cancer corpus of the uteri staging

| | |
|---|---|
| I[a]<br>IA[a]<br>IB[a] | Tumor confined to the corpus uteri<br>No or less than half myometrial invasion<br>Invasion equal to or more than half of the myometrium |
| II[a] | Tumor invades cervical stroma, but does not extend beyond the uterus[b] |
| III[a]<br>IIIA[a]<br>IIIB[a]<br>IIIC[a]<br>IIIC1<br>IIIC2 | Local and/or regional spread of the tumor<br>Tumor invades the serosa of the corpus uteri and/or adnexa[c]<br>Vaginal involvement and/or parametrial involvement[c]<br>Metastases to pelvic and/or para-aortic lymph nodes[c]<br>Positive pelvic nodes<br>Positive para-aortic nodes with or without positive pelvic lymph nodes |
| IV[a]<br>IVA[a]<br>IVB[a] | Tumor invades bladder and/or bowel mucosa, and/or distant metastases<br>Tumor invasion of bladder and/or bowel mucosa<br>Distant metastasis, including intra-abdominal metastases and/or inguinal nodes |

[a] Either G1, G2, or G3. [GX: Grade cannot be assessed; G1: Well differentiated/ less than 5% of a nonsquamous or nonmorular solid growth pattern, G2: Moderately differentiated/ 6%–50% of a nonsquamous or nonmorular solid growth pattern; G3: Poorly or undifferentiated/ greater than 50% of a nonsquamous or nonmorular solid growth pattern.

[b] Endocervical glandular involvement only should be considered as Stage I and no longer as Stage II.

[c] Positive cytology has to be reported separately without changing the stage.

The Cancer Genome Atlas (TCGA) project has categorized endometrial carcinoma into four broad categories based on integrated genomic and proteomic analyses. These are microsatellite instability cancers (1/3rd of cases; type I endometrioid tumors with high mutation rates and KRAS mutations), Microsatellite stable cancers with low copy-number alteration (associated with β-catenin gene mutations), microsatellite stable cancers with high copy-number alteration cancers (associated with TP53 mutations; serous and grade 3 endometrioid cancers) and ultrahigh mutation rate cancers (100-fold more mutation rates than low mutation tumors; associated with hotspot mutation in POLE- catalytic subunit of DNA polymerase epsilon involved in DNA replication and repair).

Four main histopathologic criteria's that have been consistently used to define high-risk disease are grade 3 tumor, presence of lymphovascular space invasion/LVSI (especially substantial/extensive), non-endometrioid histology (serous, clear cell, undifferentiated, small cell, carcinosarcoma), and cervical stromal involvement.

## Endometrial Carcinoma Treatment Approach

Understanding of molecular pathology, genetic predisposition, advanced methods of pelvic lymph nodes assessment, chemo-radiotherapy and post-procedure surveillance have shown promising results in improving survival rates in endometrial cancer cases.

The standard treatment protocol for women with endometrial cancer is surgical staging. This constitutes opening of the abdomen with a vertical midline incision, taking peritoneal washings, careful exploration of the intra-abdominal contents, careful

palpation for suspicious or enlarged nodes in the aortic and pelvic areas and an extra-fascial total hysterectomy with bilateral salpingo-oophorectomy. Adnexa should be removed irrespective of normal looking tubes and ovaries due to the possibility of micrometastases. In premenopausal women with low-grade, early-stage disease, ovaries may be preserved. In cases where cervical stroma is involved, a modified radical hysterectomy may be done. However, simple hysterectomy with free margins together with pelvic and para-aortic lymphadenectomy may be sufficient.

The final histopathology report may help guide the need for further management with radiation or chemotherapy. Table 2 highlights brief management of endometrial cancer according to stage.

**Table 2:** Management of endometrial carcinoma according to staging

| | |
|---|---|
| Stage I disease | Staging laparotomy with extrafascial hysterectomy without (grade 1 or 2 with no/superficial myometrial invasion) or with adjuvant radiotherapy.<br>High risk Stage I disease[a]- pelvic external beam radio therapy (EBRT)<br>Immediate risk factors[b]- Vaginal brachytherapy better than EBRT |
| Stage II<br>Clinically occult disease<br>Clinically bulky disease | Treatment similar to stage I<br>Higher-risk Stage II disease[a]- Pelvic EBRT |
| | Radical hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic lymphadenectomy, and selective aortic node dissection.<br>Neoadjuvant therapy followed by a less extensive simple hysterectomy is other alternative. |
| Stage III | Radical hysterectomy, bilateral salpingo-oophorectomy, , and complete surgical resection of all pelvic and/or nodal disease, followed by postoperative EBRT and/or chemotherapy. |
| Stage IV | Cytoreductive surgery with neo adjuvant chemotherapy. Neo adjuvant chemotherapy is recommended in advanced stage and relapsed disease |

[a] Grade 3 and deep invasion and/or LVSI, unfavorable histologies, unfavorable molecular factors

[b] At least two of the factors: age >60 years, deep myometrial invasion, grade 3, serous or clear cell histology, LVSI.

Hormonal therapy- In grade 1 and/or ER/ PR receptor-positive disease.

All stages, with p53abn and/or serous cancers, adjuvant chemotherapy improve survival.

If surgery is not considered feasible in advanced disease and/or in medically inoperable cases, full pelvic radiotherapy and intracavitary brachytherapy may be given preoperatively. In medically inoperable cases, primary radiation therapy may be given with clinical Stage I and II endometrial adenocarcinoma (<16% recurrence) or high dose progestin for well – differentiated adenocarcinoma, in cases where radiation therapy is not suitable.

## Summary and Recommendations

A brief summary of recommendation on management of endometrial cancers as highlighted by the Society of Gynecologic Oncology (SGO) evidence-based reviews and recommendations, part II and FIGO corpus of the cancer uteri updates, 2021 is being incorporated (*in italics*).

A. **Pelvic recurrence**

The risk of pelvic recurrence (mostly vaginal), after surgery with and without adjuvant radiation is 5% and 10-15%, respectively for intermediate risk endometrial cancer.

*In patients **not previously radiated**, pelvic radiation is recommended and can be used for nodal and/or vaginal recurrences. This should be administered as EBRT, either 3-D conformal or intensity modulated radiotherapy (IMRT), followed by brachytherapy (intracavitary or an interstitial technique) (SGO-CII).* EBRT treatment prior to brachytherapy helps in eliminating microscopic disease and shrinking gross vaginal disease. *Prior to radiation, surgical resection may be considered for isolated pelvic tumors that are resectable and not considered curable without resection (SGO-CII). Chemotherapy may be considered for those with high risk of extrapelvic relapse (SGO-CII).*

Treatment of recurrent endometrial cancer **after prior radiation** is more challenging. Pelvic exenteration may be the only curative treatment. Morbidity is high and 5-year overall survival is poor (20–60%) with pelvic exenteration.

B. **Treatment options for extra-pelvic recurrence**

1. Secondary cytoreductive surgery: It may be useful in recurrent endometrial cancer with isolated distant metastases (isolated para-aortic lymph node recurrence). However, literature support on this line of management is not very strong. *Surgery may be considered in select cases where complete surgical resection is feasible and safe. (SGO-CII).*

2. Systemic therapy:
   - Patients with recurrent endometrial cancer who have **not received prior chemotherapy** are typically treated with chemotherapy, hormonal therapy or immunotherapy. Megestrol acetate hormonal therapy, and pembrolizumab immunotherapy were the only two Food and Drug Administration (FDA) approved drugs for mismatch repair deficient recurrent tumors in the past. In 2017, FDA granted approval to pembrolizumab (anti PD-1) as the first tissue agnostic therapy for mismatch repair deficient recurrent solid tumors. Later in 2019, it approved a combination of pembrolizumab and lenvatinib for recurrent endometrial cancer without microsatellite instability-high (MSI-H) or mismatch repair deficiency (dMMR), with progressive recurrences following prior systemic therapy and not fit for surgery or radiation therapy. Hormonal treatment may be useful in low grade endometrial cancer and/or for patients who cannot tolerate chemotherapy. Megestrol acetate is most widly used and well tolerated hormonal preparation. Tamoxifen (with or without megesterol acetate), letrozole in combination with everolimus and palbocicib have also been studied.
   - With **recurrence and prior chemotherapy with a long platinum free interval**, combination platinum retreatment is recommended. Carboplatin and paclitaxel is the standard chemotherapy drug. Others single agents have also been tested in the second line.

   *Systemic therapy with chemotherapy, hormonal therapy, targeted therapy, immunotherapy, or a combination regimen, is recommended for patients with an extra-pelvic recurrence (SGO-AI, AII).*

C. **Pathologic / molecular testing considered to guide treatment**

Tumors should be tested for **mismatch repair (MMR) proteins /microsatellite instability (MSI)**. It can help guide treatment decisions and identify (on label) targeted treatment options. *MMR status and/or MSI testing should be performed on all endometrial tumors to screen for Lynch syndrome and determine eligibility for (future) single agent immunotherapy use (SGO-AI).*

***HER2Neu testing** is recommended for serous uterine cancers to determine eligibility for trastuzumab (SGO-AI, preferred).*

***Hormone receptor status** (estrogen and progesterone receptor status) should be performed to evaluate possible candidates for hormonal therapy (SGO-AII).*

***Next generation sequencing** may help identify other possible targetable mutations, especially for advanced solid tumors (SGO-BII).*

D. **Follow-up for women after treatment of endometrial cancer**

The initial 2011 SGO surveillance guidelines focused on physical examination and symptoms as primary surveillance methods. The National Comprehensive Cancer Network (NCCN) and SGO have given their separate surveillance guidelines, with a lot of similarity between the two. The SGO guidelines are based on low and high-risk characteristics of the cancer.

*A speculum and pelvic examination, in addition to a review of systems to elicit any new symptoms associated with a possible recurrence, should be completed every 3–6 months for 2 years, and every 6– 12 months thereafter in patients with endometrial cancer. Low risk endometrial cancer may be followed less frequently (e.g. every 6–12 months for first 2 years, then yearly thereafter) (SGO-CIII).* [NCCN - A physical examination every 3–6 months for 2–3 years, then 6 months or annually for all]. The SGO review recommends a thorough speculum and pelvic examination in addition to a review of systems to elicit any new symptoms associated with recurrence, such as vaginal bleeding, abdominal or pelvic pain, weight loss, headaches, coughing, or lethargy. [NCCN supplements this list with bladder or rectal bleeding, decreased appetite, shortness of breath, and swelling in the abdomen or legs.]

*Cytology (Pap tests) of the vaginal cuff should not be performed in patients with a history of endometrial cancer and no prior history of high-grade cervical dysplasia (SGO-CII).* This is because most vaginal recurrences are detected with clinical examination alone, and asymptomatic recurrences are infrequently detected with vaginal cytology.

*The NCCN and SGO recommend that radiologic evaluation such as CT or PET/CT scans should be used only if there is concern for recurrence (CIII).*

However, the NCCN notes that for patients with treated stage III-IV disease, CT of the chest, abdomen, and pelvis every 6 months is an option.

The NCCN and SGO recommend that CA-125 may be used in surveillance for those patients who have an elevated CA-125 prior to treatment. The SGO notes that the use of CA-125 may also be appropriate in patients with advanced disease or serous endometrial cancer.

SGO says that it is safe and reasonable for patients with low-risk endometrial cancer to be followed by a gynecologist once two years have elapsed from their treatment. Patients with advanced stage disease and/or high-risk histologic types should be followed by a gynecologic oncologist until five years have elapsed since their treatment, although alternating visits can be considered.

E. **Survivorship issues unique to endometrial cancer patients**

While obesity is the most common risk factor for endometrial cancer, cardiovascular disease is the leading cause of death in endometrial cancer survivors.

*Following treatment, endometrial cancer patients should be counseled on the impact of obesity, lifestyle and nutrition (SGO-CIII).*

F. **Fertility-sparing options**

14% of women with endometrial cancer are premenopausal, and 4% are less than 40 years of age. 20% of these young women may have advanced disease. Fertility preservation must be weighed over with the risk of disease progression and worsening with non-standard treatment in these women.

Common risk factors for the development of endometrial cancer in young women are increased BMI, nulliparity, irregular menstrual cycles, and polycystic ovary syndrome.

There may be an increased rate of mutations associated with Lynch syndrome in young women with endometrial cancer. Currently, the SGO and the American College of Obstetricians and Gynecologists recommend a systematic approach to identifying women with Lynch syndrome that includes either selective or universal tumor testing of endometrial carcinomas for MMR proteins or MSI testing.

While hysterectomy is considered standard of care for endometrial cancer, fertility-sparing options should be considered with appropriate counseling for a young patient desiring future fertility. Data on long term and pregnancy-related outcomes are limited.

Women with grade 1 endometrioid tumor limited to the endometrium are the best candidates for fertility sparing surgery. A dilation and curettage (D&C) is preferred for evaluating the tumor grade in these women. Endometrial biopsy may also be done.

*Patients who desire fertility sparing treatment should be evaluated by D&C (Preferred) or endometrial biopsy to evaluate grade. (SGO-AII).*

MRI is preferred for assessment for myometrial invasion and adnexal pathology in these women. Alternatively, transvaginal ultrasound can be used if MRI is not available. *An MRI to evaluate for myometrial invasion, lymphadenopathy, and adnexal pathology should also be completed (SGO-AII).*

SGO recommends tumor progesterone status assessment to identify candidates for conservative treatment. Better response rates to progesterone therapy has been reported in progesterone-positive tumors.

G. **Recommended fertility-sparing treatment of endometrial cancer.**

Progestins have been the mainstay of conservative hormonal treatment for endometrial cancer in young woman who want to preserve fertility. These progestin-based therapies include the Levonorgestrel releasing intrauterine system (L-IUS), medroxyprogesterone acetate (MPA) and megestrol acetate.

Combined oral and intrauterine progestins or hysteroscopic resection followed by L-IUS placement have also been mentioned.

*Progestin therapy with oral or intrauterine progestins should be used (SGO-AII).*

H. **Duration of conservative treatment**

Following the initiation of progestin-based therapy, it is recommended to repeat sampling with office biopsy or D&C in 3–6 months.

Hysterectomy with staging should be considered once childbearing is complete, if patients have documented progression on biopsies, and/or of endometrial cancer is still present after a specified duration of progestin-based therapy.

There is a high likelihood of requirement of assisted reproduction techniques in these women.

*Fertility sparing treatment for endometrial cancer is typically continued for 6–12 months (SGO-BII).*

*Patients will need to be thoroughly counseled about the risks and benefits of fertility sparing endometrial cancer treatment (SGO-BIII).*

I. **Ovarian preservation**

The incidence of both endometrial and ovarian cancer is significantly lower in the Lynch syndrome patients who had risk reducing surgery. Risks and benefits of ovarian preservation should be discussed with women contemplating ovarian preservation. Possibility of surgical menopause and future risk of ovarian cancer with specific mutations should also be explained to the woman. The complete fallopian tubes should be removed while preserving the ovaries.

*Ovarian preservation may be considered in premenopausal women with low grade, early stage endometrial cancer with normal appearing adnexa and no evidence of extra-uterine disease (SGO-CII).* With pelvic-confined disease, the risk of microscopic ovarian involvement is only 0.8%. The safety and benefits of ovarian preservation in younger women with early-stage endometrial cancer is well documented. Also the risk of synchronous ovarian malignancy is negligible.

*Risk-reducing hysterectomy and bilateral salpingo-oophorectomy is the recommended risk-reducing option for women with Lynch syndrome who have completed childbearing with a suggested age of 40 to 45 years old. For women considering hysterectomy with ovarian preservation, complete*

**Table 3:** FIGO recommendations, 2021 for uterine corpus cancers

| **FIGO cancer of the corpus uteri recommendations, 2021** |
|---|
| **Definitive tissue diagnosis:**<br>A definitive tissue diagnosis must be obtained preoperatively. This will result in better selection of the surgical approach and help to differentiate tumors at low-and high-risk of lymph node metastasis. Imaging might be used to determine depth of myometrial invasion, cervical involvement, and lymph node enlargement. **Level of Evidence C** |
| **Role of lymphadenectomy:**<br>Although lymphadenectomy in clinical Stage I endometrial cancer is required for staging purposes, it has no impact on overall or relapse-free survival. **Level of Evidence A**.<br>In the clinic, lymphadenectomy should be performed for staging only in high-risk cases. There is little evidence to support a therapeutic benefit, but it may be used to select women with positive nodes for adjuvant therapy and reduce the need for EBRT in node-negative patients. **Level of Evidence C** |
| **A. Adjuvant Radiotherapy:**<br>Stage I endometrial cancer with intermediate or high/intermediate risk features- Adjuvant radiotherapy has no impact on survival, but significantly reduces the rate of pelvic and para-aortic recurrence. **Level of Evidence A**.<br>Stage I high-risk patients- Vaginal brachytherapy effectively reduces the risk of vaginal relapse. **Level of Evidence A**.<br>Presumed Stage I–II disease with strong adverse factors, positive nodes, or advanced stage disease to ensure pelvic control- EBRT should be considered. **Level of Evidence A.**<br>**B. Adjuvant chemo radiotherapy:**<br>The addition of adjuvant chemotherapy to radiotherapy with high-risk disease- Improves progression-free and overall survival. **Level of Evidence A**<br>Early stage, high-risk disease with serous and/or p53abn cancers- Adjuvant chemoradiotherapy should be considered. **Level of Evidence B**<br>Adjuvant radiotherapy alone provides similar recurrence-free survival compared to three cycles of adjuvant chemotherapy and vaginal brachytherapy, with lower risk of pelvic and peri-aortic nodal recurrence. **Level of Evidence A**<br>Adjuvant chemoradiotherapy or adjuvant chemotherapy alone should be considered in patients with Stage III-IV disease and abdominal disease with residual nodules less than 2 cm diameter. **Level of Evidence A**<br>**C. Targeted therapy:**<br>It is being developed. **Professional Consensus**<br>**D. Adjuvant hormonal therapy:**<br>Use of adjuvant hormonal therapy (progestogen) has not been properly substantiated. **Level of Evidence A.**<br>**E.** Patients with endometrial cancer are frequently old and frail, and this should be taken into consideration when prescribing adjuvant therapy. **Professional consensus** |
| High-risk and advanced-stage endometrial cancer patients should be managed where possible by a gynecologic oncologist, working within a multidisciplinary team. **Level of Evidence A** |

*resection of the fallopian tubes is recommended. (SGO-AII).*

J. **Estrogen therapy for menopausal symptoms in women with history of endometrial cancer**

*In patients with low grade, early stage endometrial cancer, hormonal therapy can be considered for postmenopausal patients with severe menopausal symptoms not otherwise relieved (SGO-CII).*

K. **Position of surgical staging in women with incidental diagnosis of endometrial cancer following hysterectomy for another indication**

*Women found to have endometrial cancer incidentally after hysterectomy for other reasons should have their risk for extrauterine disease and potential for disease recurrence evaluated based on age, histologic cell type, and uterine tumor features. Individualized treatment plans can be based on the findings (SGO-B).*

L. **Radiotherapy as a primary treatment modality for endometrial cancer**

Patients who cannot undergo hysterectomy or surgical staging following a diagnosis of early stage endometrial cancer, primary RT with EBRT and intracavitary radiation may be administered for loco-regional disease control. Imaging for extrauterine disease assessment may prompt towards requirement of palliative chemotherapy after completion of radiation therapy, or for aid diagnosing advanced disease which may benefit from palliative radiation.

With high-risk histology (grade 3 endometrioid, clear cell, serous and carcinosarcoma), palliative chemotherapy can be considered. Molecular studies may also aid in planning palliative treatment with hormones or immunotherapy.

*Select women diagnosed with endometrial cancer who are not candidates for surgery can be treated with primary radiation therapy. Some patients may also benefit from chemotherapy (SGO-BII).*

## Suggested Readings


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# Update on Management of Molar Pregnancy

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Molar pregnancy or hydatidiform mole (HM) is part of gestational trophoblastic disease (GTD) which results from an aberrant fertilization and have the potential to locally invade the uterus and metastasize. It is a premalignant condition; categorized as complete mole (CHM) and partial mole (PHM).

Molar pregnancies must be managed properly to minimize acute complications and early identification of gestational trophoblastic neoplasia. Early diagnosis by ultrasound has resulted in changes in clinical presentation and decreased morbidity from uterine evacuation. The present review provides the latest concepts in its epidemiology, diagnosis, treatment and surveillance.

## Incidence

The incidence of GTD varies widely in different regions of the world (table 1).[1]

**Table 1:**

| Type | Region | Incidence |
|---|---|---|
| H mole | Europe/ North America | 0.57–1.1 per 1000 pregnancies |
| H mole | Southeast Asia and Japan | 2.0 per 1000 pregnancies |
| Choriocarcinoma | Europe/ North America | 1 in 40,000 pregnancies |
| Choriocarcinoma | Southeast Asia and Japan | 9.2 and 3.3 per 40,000 pregnancies |

## Risk Factors for Molar Pregnancy

The main risk factors for HM are extremes of maternal age and a history of previous mole.

A. Maternal age: The risk increases after 35 years of age and there is a 5–10 times increased risk after 45 years. Teenagers have a two-fold risk of having a molar pregnancy.
B. Previous molar pregnancy: Mutations in *NLRP7* and *KHDC3L* have been reported in women with recurrent molar pregnancy.[2]
   - Recurrence rate after previous one mole: 10 times compared to that for general population.[2]
   - Recurrence rate after two molar pregnancies: 11 to 25 percent.
C. History of prior spontaneous abortion increases the risk of molar pregnancy (both complete and partial) 2 to 3 fold compared to women without a history of prior miscarriage.
D. Dietary deficiency of beta-carotene and animal fat is considered to be etiological factor for complete mole, but not for partial mole.

## Classification of Hydatidiform Mole

Partial and complete hydatidiform moles are distinct diseases (Table 2).[3] There is a defect in gametogenesis

**Table 2:** Features of Complete and Partial Moles

| Feature | Complete Mole | Partial Mole |
|---|---|---|
| **Karyotype** | 46, XX or 46, XY Paternal origin<br>• *NLRP7 & KHDC3L* germline mutations in patients result in biparental normal chromosomal compliment & are responsible for recurrent moles | 69, XXX or 69, XXY 2/3 paternal, 1/3 maternal origin |
| **Pathology** | | |
| Evidence of fetus | Absent | May be present |
| Amnion, fetal RBCs | Absent | Present |
| Villous edema | Diffuse, markedly edematous avascular hydropic villi with sheets of trophoblastic cells at the periphery | Variable edema of the villi, with scalloping at the edges and trophoblastic inclusions within villi. |
| Trophoblastic proliferation | Diffuse | Focal |
| p57 staining | Absent | Present |
| **Clinical Presentation** | | |
| Clinical diagnosis | Molar gestation or missed abortion | Missed abortion |
| Uterine size | Up to 50% large for dates | Small for dates |
| Theca lutein cysts | 9–25% | Rare |
| Medical complications | 6–20% | Rare |
| Post-molar GTN | 15–20% | 0.5–5% |

or fertilization in both the conditions because of which the placental villi become edematous, forming small grape-like (hydatidiform) structures.

Complete molar pregnancies are diploid and androgenic in origin, with no evidence of fetal tissue. Complete molar pregnancies usually (75–80%) arise as a result of duplication of a single sperm following fertilisation of an 'empty' ovum. Some complete moles (20–25%) can arise after dispermic fertilisation of an 'empty' ovum.

Partial molar pregnancies are usually (90%) triploid in origin, with two sets of paternal haploid chromosomes and one set of maternal haploid chromosomes. Partial molar pregnancies occur, in almost all cases, following dispermic fertilization of an ovum.

Women with consecutive molar pregnancies should undergo germline genetic testing for mutations in NLRP7 and KHDC3L, because these mutations are identified in more than half of such women. p57 staining is present both in partial mole and non-molar gestation, hence cannot differentiate PHM from spontaneous hydropic abortion but can be helpful in differentiating CHM from PHM.

## Clinical Features

Hydatidiform moles are usually diagnosed during the first half of pregnancy. Abnormal vaginal bleeding is the most common presenting symptom, occasionally associated with passage of hydropic villi. If there is vaginal passage of the gestational product, vesicles may be seen. Other classic signs and symptoms include uterine enlargement greater than expected for gestational dates, cystic enlargement of the ovaries (theca lutein cysts), hyperemesis gravidarum, pregnancy-induced hypertension in the first trimester, and an abnormally high level of hCG for gestational dates.

As diagnosis is often made in the first trimester with ultrasound examination, complications such as hyperemesis gravidarum, pre-eclampsia, and hyperthyroidism are less common.

## Diagnosis of Hydatidiform Mole

The possibility of HM should be considered in any reproductive age female with abnormal vaginal bleeding. Human chorionic gonadotropin (hCG ) is the biomarker of disease. Ultrasound examination is imaging of choice in establishing the diagnosis of molar pregnancy. The combination of ultrasound findings with elevation of hCG above expected for gestational age is highly suggestive of molar pregnancy.

## Sonographic Features

*Complete mole*: Absence of an embryo or fetus; Absence of amniotic fluid; Central heterogeneous mass with numerous discrete anechoic spaces – This has classically been described as a "snowstorm or Swiss cheese pattern"; Ovarian theca lutein cysts.

*Partial mole:* Partial mole is difficult to diagnose on ultrasound. A fetus may be present, but may be growth restricted or have low amniotic fluid. Characteristic sonographic findings are present in a minority of cases.

## Histological Examination

The definitive diagnosis of a molar pregnancy is made by histological examination.

Complete or partial mole will sometimes be diagnosed only by pathology after dilation and evacuation (D & E) is performed for a suspected incomplete abortion. In these cases, patients should be monitored afterwards with serum quantitative hCG values.

If no fetal parts are identified at the time of abortion or on prior ultrasound then the products of conception following medical or surgical management of all miscarriages should be examined histologically. Following miscarriage woman should be advised to do a urinary pregnancy test 3 weeks after miscarriage. [4]

## Management of Hydatidiform Mole

Suction evacuation is the method of choice for management of molar pregnancy. It is usually performed under ultrasound guidance.

### *Pre-evacuation Evaluation*

***Biochemical tests and imaging as following:*** Serum quantitative β-hCG, Complete blood count, clotting studies (PT and PTT), renal and liver functions, blood group and screen, Ultrasound pelvis, Chest X-ray, Thyroid function tests in patients with symptoms of hyperthyroidism

### *Evacuation*

The procedure is usually performed under general anesthesia, but local or regional anesthesia may be used for a cooperative patient with a small uterus. It should be done under ultrasound guidance where available and includes following steps:

A. Serial dilation of cervix without sounding the uterus (*Ripening of cervix with either mechanical dilators or prostaglandins prior to suction evacuation is not associated with an increased risk of developing GTN, hence it's safe to use them).*
B. Number 10, 12 or 14 suction cannula is introduced.
C. It's our practice to start Oxytocin 10 units/500ml infusion once karman's cannula has been introduced after cervical dilatation. This decreases the blood loss and risk of perforation. Oxytocin infusion is continued for several hours after evacuation if there is significant uterine bleeding after D&E & other oxytocics such as methergine can be used. However, RCOG guidelines do not recommend the routine use of oxytocin before the completion of evacuation for the risk of trophoblastic embolization.
D. Complete evacuation with suction cannula.
E. Role of sharp curettage unclear. This may increase the risk of uterine perforation and risk of uterine synechiae.

***Management After Evacuation***

A. Products of conception must be sent for histopathological examination.
B. Anti D if Rh-negative: Anti D should be given to Rh-negative women after molar evacuation because the RhD factor is expressed by trophoblast.
C. Serial $SpO_2$ monitoring in patients with uterine enlargement greater than 14 weeks in size: Pulmonary complications are observed at the time of molar evacuation in less than 1% of patients but in patients with uterine enlargement greater than 14–16 weeks in size this complication is observed in more than 20% necessitating the need for $SpO_2$ monitoring.[3]
D. Post evacuation hCG: hCG is used for post-treatment surveillance to look for response or progression of disease and to plan subsequent management accordingly.

## Role of Hysterectomy

Hysterectomy should be considered in women older than age 40 years of age. Hysterectomy is an alternative to suction curettage if childbearing is complete. It provides permanent sterilization and decreases the need for subsequent chemotherapy by eliminating the risk of local myometrial invasion as a cause of persistent disease.

*Induction of labor and hysterotomy are not recommended for molar evacuation, since, these methods increase maternal morbidity and the development of postmolar GTN requiring chemotherapy.*

## Surveillance after Molar Evacuation

Progression of CHM and PHM to GTN occurs in 15%–20%, and 0.5%–5% of cases, respectively.[4]

Serial quantitative serum hCG monitoring should be performed after molar evacuation. For monitoring patients with gestational trophoblastic disease, an hCG assay that can detect all forms of hCG is needed because these neoplasms often secrete abnormal forms of hCG like free beta, nicked-free beta, C-terminal hCG, beta core and hyperglycosylated hCG.

Ideally, serum hCG levels should be obtained within 48 hours of molar evacuation and followed every 1–2 weeks. For complete molar pregnancy, if hCG has reverted to normal within 56 days of the pregnancy event then follow-up should be for 6 months from the date of uterine evacuation.[4] If hCG has not reverted to normal within 56 days of the pregnancy event then follow-up should be for 6 months from normalisation of the hCG level.[4]

Follow-up for partial molar pregnancy is concluded once the hCG has returned to normal on two samples, at least 4 weeks apart.[4]

## Role of Repeat Evacuation

There is a role for urgent surgical management for the woman who is experiencing heavy or persistent vaginal bleeding causing acute haemodynamic compromise, particularly in the presence of retained pregnancy tissue on ultrasound.

## Role of Prophylactic Chemotherapy

Prophylactic administration of either methotrexate or actinomycin D chemotherapy at the time of or immediately following molar evacuation is associated with a reduction in the incidence of postmolar GTN to 3%–8%. However, prophylactic chemotherapy may increase drug resistance and is associated with toxicities. It should be limited to situations in which the risk of postmolar GTN is much greater than normal or where adequate hCG follow-up is not possible.[5]

## Twin Pregnancy with One Mole (CMF- Co-existent Mole & fetus)

Molar pregnancy rarely coexists with a normal pregnancy; developing in only 1 per 22,000 to 100,000 pregnancies.[6] The diagnosis is usually made on ultrasound. Although there is a high risk of spontaneous abortion, about 40%–60% result in live births. Patients should be advised of the potential risks, including: (1) severe complications such as preeclampsia, hemorrhage, and thyrotoxicosis, which typically develop in the second trimester; (2) preterm delivery; and/or (3) malignancy, gestational trophoblastic neoplasia (GTN).

The risk of GTN in coexisting molar and normal pregnancy ranges from 27% to 46%.[2]

In the absence of complications and normal genetic and ultrasound findings; pregnancy can be continued. Prenatal invasive testing for fetal karyotype should be considered in cases where it is unclear if the pregnancy is a complete mole with a coexisting normal twin or a possible singleton partial molar pregnancy.

For twin pregnancies where there is a non-molar pregnancy alongside a molar pregnancy and the woman has decided to terminate the pregnancy (or there has been demise of the coexisting twin) and the size of the fetal parts is big for the use of suction curettage, medical removal can be used.

In authors' experience, two cases CMF have been managed. In both the cases suction evacuation was done for H mole under ultrasonic guidance with aspirotomy of the second fetus at 14 weeks.

## Subsequent Pregnancy

Women who have had a removal of a molar pregnancy are advised not to become pregnant until they have completed their hCG follow-up. All future pregnancies should be evaluated by a first-trimester obstetric ultrasound examination. The risk of repetitive molar pregnancies increases substantially if woman has had two or more prior moles. Women who have not received chemotherapy no longer need to have hCG measured after any subsequent pregnancy event.

## Postmolar Gestational Trophoblastic Neoplasia (GTN)

Patients are at increased risk for postmolar gestational trophoblastic neoplasia if they have any of the following: Age older than 40 years; Pre evacuation hCG greater than 100,000 mIU/ml; Excessive uterine enlargement; Theca lutein cysts greater than 6 cm.

Post-molar GTN is usually diagnosed by hCG surveillance. In 2000, FIGO standardized the hCG criteria for the diagnosis of post-molar gestational trophoblastic neoplasia which is summarized in Table 3.

**Table 3:** Diagnostic Criteria for Post Molar Gestational Trophoblastic Neoplasia[7]

| |
|---|
| I. hCG criteria after molar evacuation |
| a. Sustained hCG level plateau ± 10% for four measurements over a period of 3 weeks or longer, that is day 1, 7, 14, 21. |
| b. Sustained hCG level rise greater than 10% of 3 values over a 2-wk duration |
| c. Persistence of detectable hCG more than 6 months after molar evacuation |
| II. Presence of metastatic disease |
| III. Histologic diagnosis of GTN |
| a. Invasive mole |
| b. Gestational choriocarcinoma |
| c. Placental site trophoblastic disease |
| d. Epithelioid trophoblastic disease |

## Contraceptive Advice

Patients with HM must be advised to use reliable contraception during the entire period of postoperative hCG monitoring. Options include hormonal contraception (progestin-only or combined estrogen-progestin) or barrier methods.[8] Oral contraceptives after molar evacuation as compared with barrier methods do not increase the risk for or clinical aggressiveness of GTN when adjusted for risk factors. Centers for Disease Control and Prevention recommends not inserting an intrauterine device (IUD) in patients with persistently elevated hCG levels because of theoretical risk for perforation, infection, and hemorrhage.[8] An IUD may be used in patients with confirmed GTD with undetectable or decreasing hCG levels.

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# Approach to an Adnexal Mass

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## Introduction

An adnexal mass is a common gynecological problem seen in women of all ages with varied causes (Table 1). Ovarian masses are identified in approximately 8-35% of premenopausal patients and 3-17% of postmenopausal patients.[1]Many of these are found incidentally on ultrasound scan in asymptomatic women.

## Aims of Evaluation of Adnexal Mass are

- To know if the mass is "almost certainly benign," or has a "reasonable chance of being malignant,"
- To determine whether there is an urgent condition or hemodynamic instability that requires prompt surgical treatment.

## History

*Age*- The etiology, prognosis and management of adnexal mass varies in different age groups. Adolescents and reproductive age women mostly have benign masses. While germ cell tumors are common in 10-30 year age group, epithelial tumors are seen in postmenopausal women.

*Symptoms of adnexal mass*- Patients with an adnexal mass may be asymptomatic or present with pelvic pain or pressure, abdominal fullness or pressure, gastrointestinal discomfort (nausea, vomiting, constipation, bloating), difficult or frequent urination, dysmenorrhea, dyspareunia, fever or abnormal uterine bleeding (AUB).

Pelvic pain or pressure is the most common symptom. It is often unilateral and can be of variable severity,

**Table 1:** Etiology of Adnexal Masses

| Gynecological Causes | | | Nongynecological Causes |
|---|---|---|---|
| Ovarian | Tubal | Others | |
| **Benign** | | | |
| Functional (physiological) cyst<br>Corpus luteal cyst<br>Luteoma of Pregnancy<br>Theca lutein Cyst<br>Ovarian Ectopic Pregnancy<br>Polycystic Ovaries<br>Endometrioma<br>Cystadenoma<br>Benign Ovarian Germ Cell Tumor (Eg-Mature Teratoma)<br>Benign Sex Cord Stromal Tumor | Ectopic Pregnancy<br>Hydrosalpinx | Paraovarian Cyst<br>Paratubal Cyst<br>Uterine leiomyoma (pedunculated/ cervical)<br>Broad Ligament Leiomyoma<br>Tuboovarian Abscess | Constipation<br>Appendiceal abscess<br>Diverticular Abscess<br>Pelvic Abscess<br>Bladder Diverticulum<br>Ureteral Diverticulum<br>Pelvic Kidney<br>Peritoneal Cyst<br>Nerve Sheath Tumor |
| **Malignant or Borderline** | | | |
| Epithelial Ovarian Carcinoma<br>Epithelial Borderline Neoplasm<br>Malignant Ovarian Germ Cell Tumor<br>Malignant Sex Cord Stromal Tumor | Epithelial Carcinoma Serous Tubal Intraepithelial Neoplasia | Metastatic Endometrial Carcinoma | Appendiceal Neoplasm<br>Bowel Neoplasia<br>Retroperitoneal Sarcoma<br>Metastasis from Breast, Colon, Lymphoma |

**Table 2:** Factors affecting Risk of Ovarian Cancer

| **Risk Factors** | **Relative Risk[3]** | **Protective Factors** | **Relative Risk[3]** |
|---|---|---|---|
| Infertility | 2.67 | Past use of OCP | 0.73 |
| Endometriosis (Risk for clear cell, endometrioid, low grade serous carcinoma) | 2.04 to 3.05 | Past breast feeding for >12 months | 0.72 |
| Smoking (Risk for mucinous carcinoma) | 2.1 | Tubal ligation | 0.69 |
| Gene mutation (BRCA 1, BRCA 2, BRIP1, RAD51C, RAD 51D), Lynch Syndrome | | Previous pregnancy | 0.71 |

acute or gradual onset, sharp or dull, and constant or intermittent. More generalized pain may occur if an adnexal cyst ruptures and spills irritants (eg, blood, sebaceous material, inflammatory contents) into the peritoneal cavity. AUB is seen in ectopic pregnancy, sex cord-stromal tumors. Associated infertility and dysmenorrhoea is seen in endometriosis.

Symptoms of ovarian cancer vary from abdominal (77%), gastrointestinal (70%), pain (58%), constitutional (50%), urinary (34%) or pelvic (26%) complaints.[2]

*Factors affecting risk for Ovarian Cancer*- Factors that affect the risk of ovarian cancer are as given in table 2.

*Family History*- A woman with a first-degree relative (mother, father, sister, brother, daughter or son) affected by breast, colon, ovarian, endometrial cancer is at high risk of ovarian cancer.

## Physical Examination

General examination may reveal cervical lymphadenpathy (Tuberculosis, Ovarian Malignancy), unilateral edema or varicose veins (large adnexal mass), hepatomegaly (liver metastasis), virilisation (sex cord stromal tumors).

*Per abdominal examination*- to look for abdominal distention, ascites, or a palpable mass.

*Pelvic examination* is important to assess a palpable mass for size, consistency, tenderness, mobility, nodularity and ascites. Findings such as pain with palpation; or a mass that is irregular, fixed, and/or associated with posterior cul-de-sac nodularity indicate endometriosis or ovarian malignancy.

Pelvic examinations, including a rectal exam, even under anaesthesia, have only 15-51% sensitivity to identify an adnexal mass, especially with BMI>30.[4] Small adnexal masses may be difficult to palpate due to the deep anatomic location of the ovary. Larger masses can extend out of the pelvis and be difficult to feel. In patients with a prior hysterectomy, the ovaries may rise out of the pelvis and be difficult to palpate due to loss of ligamentous attachments.

History of gastrointestinal malignancy, younger age, absence of ascites, bilateral solid adnexal mass is suggestive of metastasis to ovary.

## Evaluation

A positive pregnancy test would indicate an ectopic pregnancy(ovarian/tubal) or luteoma of pregnancy.

## Estimation of Risk of Malignancy

Over 80 different models, using serum biomarkers, imaging features, and other factors like menopausal status, have been proposed to estimate the risk off malignancy.

1. **Simple models-** Use discrete cut-off values such as CA-125, Pulsatility Index, and Resistance Index.
2. **Intermediate models-** Include morphology scoring systems, Risk of Malignancy Index (RMI)
3. **Advanced models** include artificial neural networks and multiple logistic regression models – a method for determining whether each of a set of independent variables has a unique predictive relationship to a dichotomous dependent variable. However, their use is restricted to centers having the special software.

A. **Serum tumor markers**– Their utility in risk assessment for malignancy is limited. However, if positive, they can be used for monitoring disease response to treatment.

   1. *Cancer antigen 125 (CA 125)*- At a cutoff of 35IU/ml, CA125 has a sensitivity and specificity of 78%. It should be the only serum marker used for primary evaluation in adnexal masses suspicious of epithelial ovarian cancer (EOC).

      Limitations: It is raised in over 80% of epithelial ovarian cancer cases, but not in most primary mucinous ovarian cancers. It is nonspecific and seen in many non-malignant conditions (Table 3) with poor specificity for premenopausal women. It is measured in all postmenopausal women with an adnexal mass, however it is of no value in premenopausal women with simple ovarian cyst.[4]
   2. *HE4* is a glycoprotein found in epididymal epithelium. Increased serum HE4 levels and expression of the *HE4* (*WFDC2*) gene occurs in ovarian cancer, as well as in lung, pancreas, breast, bladder/ureteral transitional cell and endometrial cancers. It is not increased in endometriosis and is therefore, more sensitive and specific than CA125 for the diagnosis of ovarian cancer, especially in premenopausal women with increased CA125 due to endometrioma. However, data is not substantial enough to suggest its routine clinical use.
   3. *Lactate dehydrogenase (LDH), α-FP and hCG* should be measured in all women under age 40 with a complex ovarian mass because of the possibility of germ cell tumours.

**Table 3:** Differential Diagnosis for CA125

| Increase CA125 |
|---|
| Gynaecological Malignancies<br>Epithelial ovarian, fallopian tube, primary peritoneal cancers; Endometrial Cancer |
| Benign Gynaecological Conditions<br>Menstruation, Pregnancy<br>Functional ovarian cysts<br>Benign Ovarian Neoplasms<br>Pelvic Inflammatory Disease<br>Fibroid, Endometriosis, Adenomyosis<br>Acute events in Benign Cysts (Torsion, Haemorrhage) |
| Nongynecological Conditions<br>Peritoneal irritation (tuberculosis, cirrhosis, ascites, hepatitis, pancreatitis, colitis, peritonitis, pleuritis, Meigs syndrome, Ovarian Hyperstimulation, Tuberculosis peritonitis)<br>Heart Failure, Myocardiopathy, Myocardial Infarction, Pericardial disease<br>Cystic Fibrosis, Pleural Effusion, Pneumonia, Pulmonary Embolism, Sarcoidosis, SLE<br>Renal Insufficiency, Urinary Tract Infection<br>Recent Surgery |
| Nongynecological Cancers<br>Primary tumours that metastasise to peritoneum (breast, lung, liver, pancreas, gall bladder, colon cancer) |
| Decrease CA125 |
| Smoking, Caffeine intake, Hysterectomy |

4. Elevated **CEA (>5ng/ml)** and **CA19-9 (>37IU/ml)** suggest primary mucinous cystadenoma of ovary. Besides, raised CEA can also be seen in ovarian metastasis from gastrointestinal malignancies. Sometimes, CA19-9 can be raised in mature cystic teratomas of the ovary. However, both these markers are nonspecific with conflicting results. Panels including multiple other tumour markers ***(CDX2, CA72-4) do not*** offer any further advantage in the initial assessment of ovarian cysts. Thus, the use of tumour markers is more for follow up, rather than diagnosis.

B. **Imaging**

1. *Transvaginal pelvic ultrasound* using multifrequency probes by trained clinicians is the single most effective way of evaluating an adnexal mass. Transabdominal ultrasound should be used to provide supplementary information to transvaginal ultrasound particularly when an ovarian cyst is large or beyond the field of view of transvaginal ultrasound. Ultrasound identification of a simple cyst establishes a benign process in 95–99% of postmenopausal women.

   'Pattern recognition' of specific ultrasound morphological findings with more complex scoring systems especially when performed by more experienced clinicians can produce sensitivity and specificity equivalent to logistic regression models and avoid 'unnecessary' surgical interventions.

2. *IOTA group simple ultrasound rules*

   A detailed ovarian cyst classification system developed by the consensus group from the International Ovarian Tumor Analysis (IOTA) group in 2000, defines ovarian mass in following terms (Figure 1):

   1. Unilocular, unilocular-solid, multilocular, multilocular-solid or solid
   2. Cyst contents – anechoic, low level, ground glass, haemorrhagic or mixed
   3. Solid material or papillary structures (solid protusion>3mm) or wall irregularity (solid protusion <3mm)
   4. Vascularity on Color Doppler (No flow=1, Minimal flow=2, Moderate flow=3, Strong flow throughout =4)
   5. Shadows
   6. Ascites- Fluid outside POD[8]

   **Two Step Strategy:** (Sensitivity 95%, Specificity 91%, PPV 80.9%, NPV 97.6%). If the mass is not instantly recognisable and Simple Descriptors (SD) does not apply, then Simple Rules (SR) (Table 4) is applied.

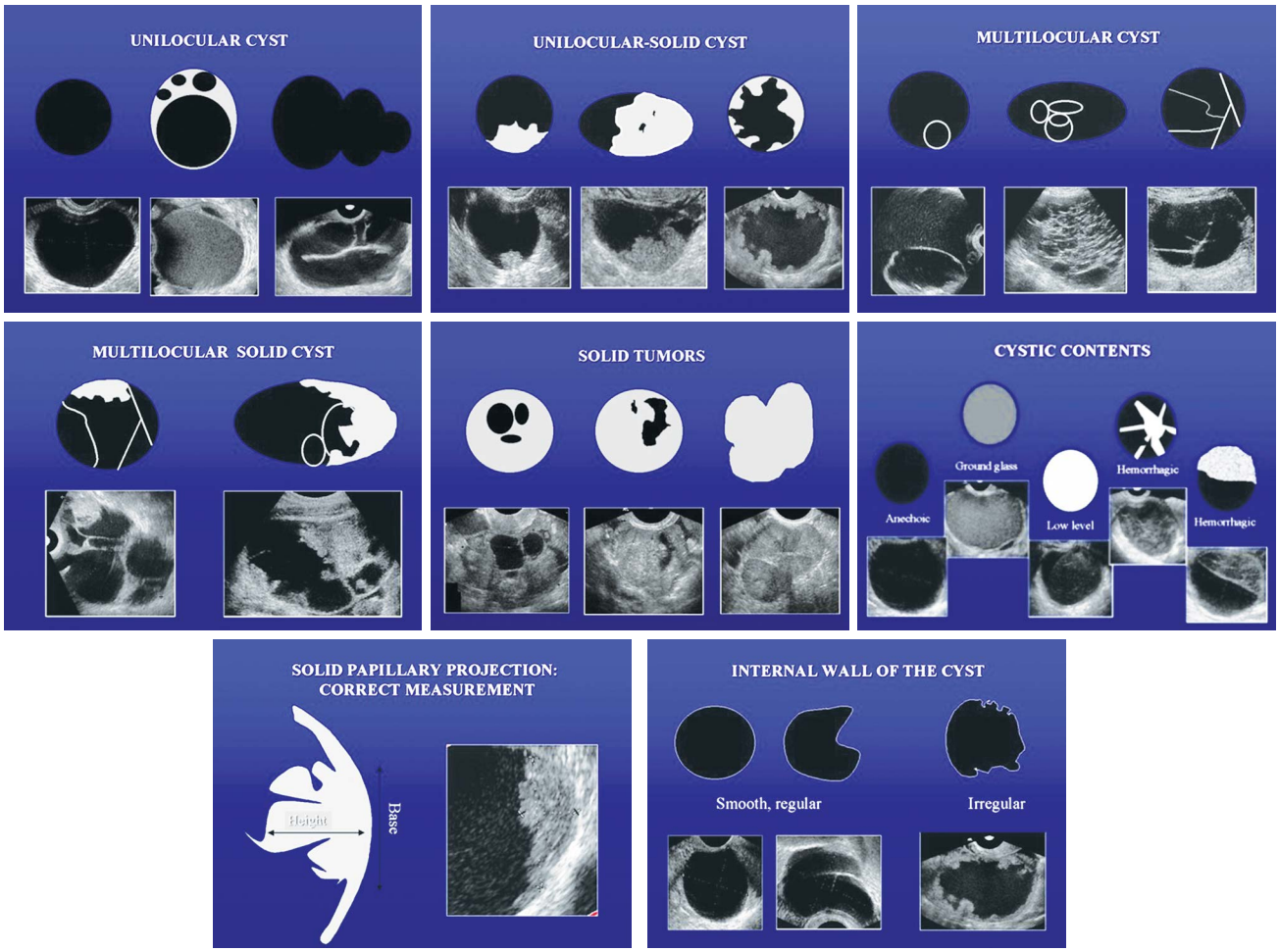


**Fig 1:** IOTA Definitions

**Table 4:** IOTA Simple Rules

| Benign Rules | Malignant Rules |
|---|---|
| **B1** Unilocular cysts<br>**B2** Presence of solid components where the largest solid component < 7 mm<br>**B3** Presence of acoustic shadowing<br>**B4** Smooth multilocular tumour with largest diameter < 10cm<br>**B5** No blood flow on colour Doppler. | **M1** Irregular solid tumour<br>**M2** Ascites<br>**M3** At least 4 papillary structures<br>**M4** Irregular multilocular solid tumour with largest diameter ≥ 10cm<br>**M5** Prominent blood flow on colour Doppler with color flow score 4 |
| Rule 1: If ≥1 B-features, with no M-features: Benign<br>Rule 2: If ≥1 M-features, with no B-features: Malignant<br>Rule 3: If combination of both B-and M-features are present: Inconclusive 9 | |

**Alternative 2 Step Strategy**- Using simple rules, Simple Rules risk (SR risk) calculator tool helps in segregating patients into specific malignancy risk categories for assigning the appropriate level of clinical/surgical management (Table 5). It is also proposed to be the next best alternative to the three step strategy.[10,11]

**Table 5:** IOTA simple rules risk calculator (SR risk) mode

| Features | Risk Stratum | Estimated Risk of Malignancy |
|---|---|---|
| >2 B-Features | Very Low Risk | 0.01 to 0.29% |
| Only B1 or only 2B-features | Low Risk | 0.19 to 3.1% |
| Only 1 B-feature (other than B1) | Intermediate Risk | 2.4 to 15.2% |
| 2 sub-categories (both M- and B-features)<br>Equal no. of M- and B-features<br>More B-features than M-features | Elevated risk | 2 sub - categories:<br>5.6 to 78.1%<br>1.3 to 28.4% |
| More M-features than B-features | Very high risk | 42 to>99.9% |

**Three Step Strategy-** For masses classified as

*to be continued on.....page 34*

*continued from..... on page 32*

"inconclusive" by Simple Rules at the "second step", Real time Subjective assessment (SA) by an expert examiner forms the "third step"

3. **O-RADS** —In 2020, American College of Radiology (ACR) gave the Ovarian-Adnexal Reporting and Data System (O-RADS) system (1-5) for risk stratification and management of adnexal masses, based on USG features.[12] These categories and malignancy risk estimates are shown in Table 6.

While the O-RADS system is new, it is founded on years of data established by IOTA and other studies, and appears to compare favourably with other established classification systems. Though, the O-RADS system is promising, yet not widely used.

**3D scans do not improve diagnostic accuracy.**

**Table 6:** O-RADS Stratification and Management System

| **O-RADS RISK CATEGORY** |
|---|
| **O-RADS 0 INCOMPLETE EVALUATION** |
| **O-RADS 1 NORMAL OVARY** Follicle defined as a simple cyst ≤3cm |
| **O-RADS 2 ALMOST CERTAINLY BENIGN (<1% Risk of Malignancy)**<br>• **Simple Cyst***<br>• **Classic Benign Lesions#**<br>• **Nonsimple unilocular cyst, smooth inner margin** |
| **O-RADS 3 LOW RISK of Malignancy (1 to <10% Risk of Malignancy)**<br>• Unilocular Cyst ≥10cm (simple or nonsimple)<br>• Typical Dermoid Cysts, Endometrioma, Haemorrhagic Cyst ≥10cm<br>• Unilocular Cyst, any size with irregular inner wall <3mm<br>• Multilocular Cyst 10cm, smooth inner wall, CS=1-3$^{\$}$<br>• Solid, smooth, any size, CS=1 |
| **O-RADS 4 INTERMEDIATE RISK (10 to <50% Risk of Malignancy)**<br>• **Multilocular Cyst, No Solid Component**<br>≥10cm, smooth inner wall, CS=1-3<br>Any size, smooth inner wall, CS=4<br>Any size, irregular wall and/or irregular septation, any CS<br>• **Unilocular Cyst with solid component** Any size, 0-3 papillary projections, CS=any<br>• **Multilocular Cyst with solid component** Any size, CS=1 to 2<br>• **Solid** Smooth, Any size, CS=2 to 3 |
| **O-RADS 5 HIGH RISK (≥50% Risk of Malignancy)**<br>• Unilocular Cyst, any size, ≥4 papillary projections, CS=any<br>• Multilocular Cyst with solid component, any size, CS=3 to 4<br>• Solid smooth, any size, CS=4<br>• Solid Irregular, any size, CS=any<br>• Ascites and/or peritoneal nodules |

**MRI, CT, and PET-CT are not recommended for the initial evaluation of ovarian cysts.** Contrast enhanced MRI (ADNEX MRI Score 1-5) is used when USG cannot conclusively characterize mass as benign or malignant. **CECT** has low specificity for characterising ovarian mass, but is used to evaluate the abdomen for metastases and stage a primary ovarian malignancy or when nongynaecologic origin of an adnexal cyst is suspected. **PET-CT** is used to identify other sites of metastasis in an advanced ovarian malignancy and monitor response to chemotherapy.

C. **Multimodal Tests –**

1. **OVA1**

   OVA1 is a quantitative assay that measures 5serum proteins (**CA125, transthyretin [prealbumin]**, **apolipoprotein A1, beta-2-microglobulin and transferrin**) and combines them into a numerical score (0-10) using a special software (OvaCalc®). A value higher than 5 in premenopausal and 4.4 in postmenopausal woman is indicative of a high risk of malignancy. Although OVA1® has a high sensitivity, it shows a lower specificity and positive predictive value than the RMI.[5]

2. **ROMA** (Sensitivity 89%, Specificity 83% )

   ROMA is a quantitative test that uses **CA125, HE4** and **menopausal** status and combines them into a numerical score using an algorithm. A cut-off of 2.27 represents a high risk of malignancy. It should be interpreted along with clinical and radiological features not intended to be a screening or a standalone diagnostic assay. However, data on HE4 is not enough.[6]

3. **Risk of Malignancy Index, RMI**

   The RMI is calculated as a product of three presurgical features– RMI = CA125× M × U

   a. Serum **CA125** is measured in IU/ml.

   **b. Menopausal status (M):** 1 = premenopausal, 3= postmenopausal

   **c. USG (U):** The ultrasound result is scored 1 point for each of the following characteristics: Multilocular cysts, Solid areas, Metastases, Ascites, Bilateral lesions.

   U = 0 (for USG score of 0), U= 1 (for USG score of 1), U= 3 (for USG score of 2–5).

At a threshold of **200**, RMI has a sensitivity of 78% and specificity of 87%. At present RMI is the most widely used model but recent studies have shown

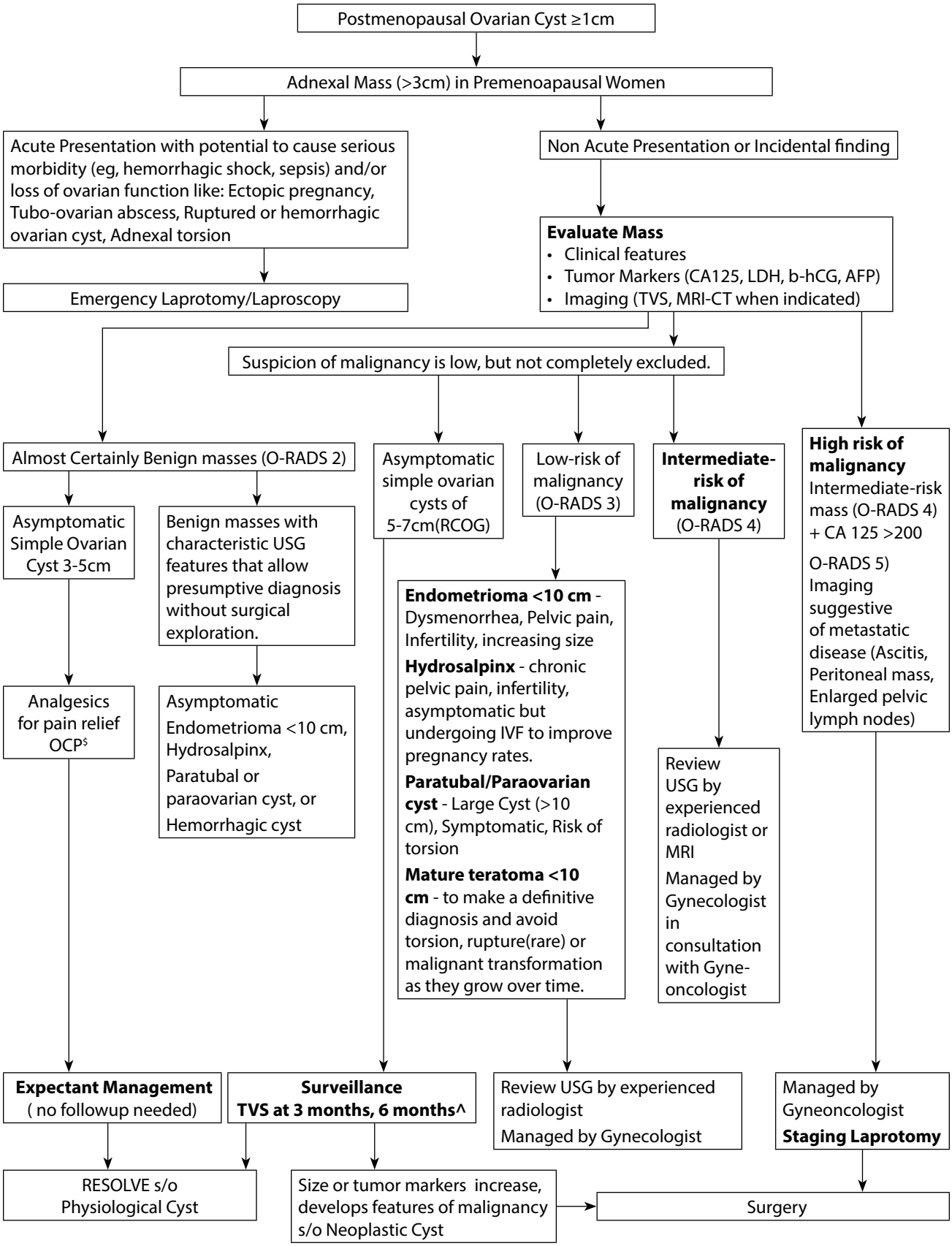


**Fig 2:** Management of Adnexal Mass in Premenopausal Patient

$ OCP do not decrease size of existing cyst, but inhibit ovulation and prevent the formation of new symptomatic physiologic ovarian cysts, while the existing cyst resolves.

^ There is no consensus regarding surveillance frequency.

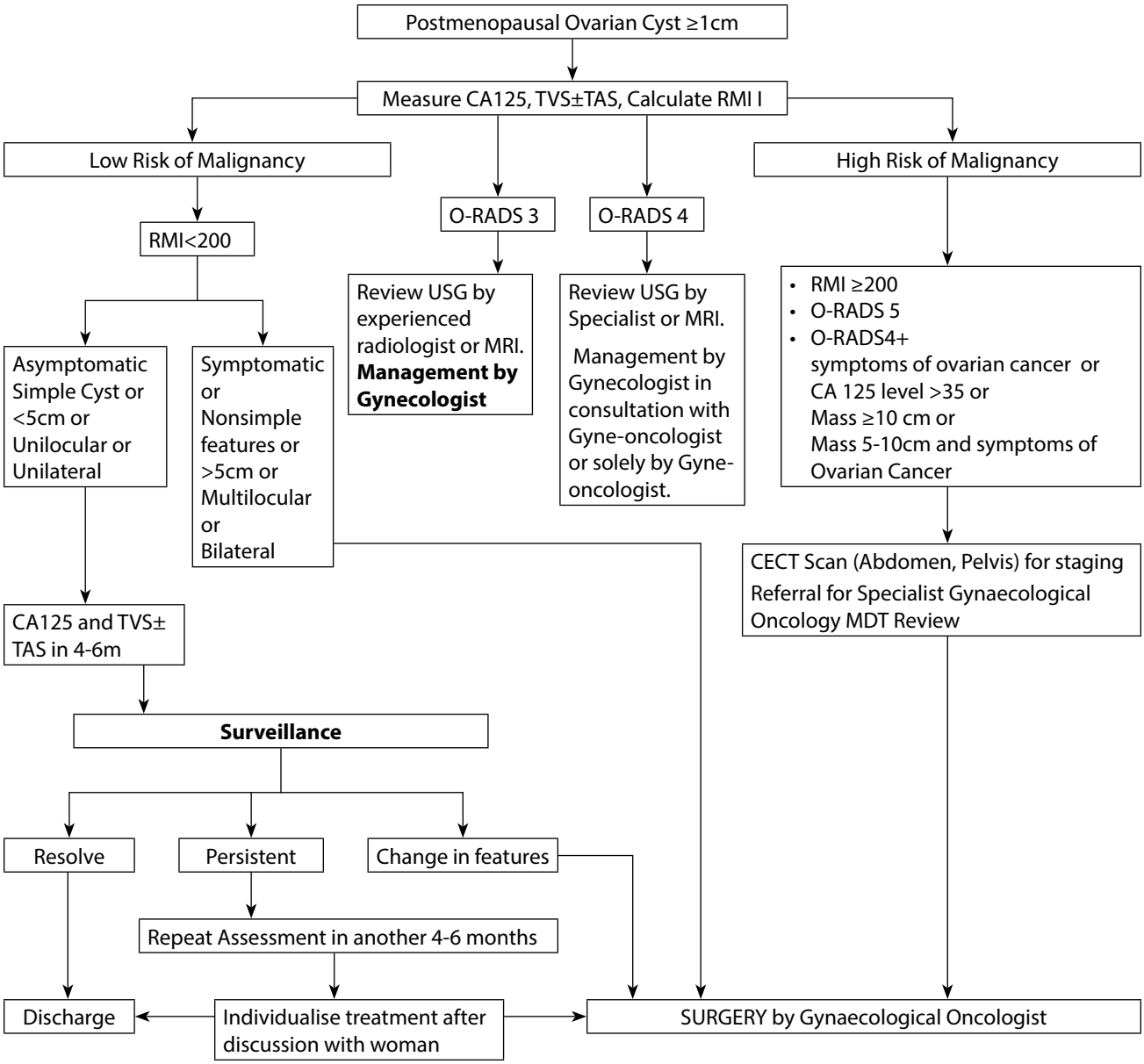


**Fig 3:** Management if Adnexal Mass in Postmenopausal Patients

*In postmenopausal women, there is no role of cystectomy. Unilateral oopherectomy with bilateral salpingectomy is done. Bilateral salpingectomy can decrease the risk of developing ovarian cancer. Removal of the contralateral ovary depends on patient age, years since menopause, patient's choice, desire to avoid subsequent surgery for additional adnexal pathology, and threshold for long-term health risks following bilateral oophorectomy.

#laparotomy through a midline incision with clear documentation, cytology – ascites or washings, total abdominal hysterectomy, bilateral salpingo-oophorectomy and omentectomy, biopsies from any suspicious areas, bilateral selective pelvic and para-aortic lymphadenectomy can be considered.

the IOTA classification, which is based on specific ultrasound parameters, has better sensitivity and specificity to RMI and forms an alternative for those experienced in this technique.

**Diagnosis**: A **presumptive** diagnosis of the **etiology** of an adnexal mass can often be made based on the classic sonographic appearance of the mass, further supported with history and clinical findings. A **definitive** diagnosis of the **etiology** of an adnexal mass is made by characteristic histologic findings following surgery.

Image-guided biopsy of the adnexal mass i**s not** recommended as incising or rupturing the mass can cause spillage of malignant cells into the peritoneum and advance the stage of primary cancer. It is useful in advanced stage when neoadjuvant chemotherapy is planned. Cytological examination of aspirated ovarian cyst fluid has only 25% sensitivity in distinguishing benign and malignant tumours.

## Management

Surgery is required when there is a high risk of malignancy, histologic diagnosis is desired, or the patient has persistent pain or other symptoms. The type of surgery (e.g. ovarian cystectomy, oophorectomy, staging procedure) and surgical approach (i.e. laparoscopic versus open) is based on many factors, including patient age, desire for future childbearing, degree of suspicion for malignancy, and intraoperative findings (including frozen section assessment, if performed). The management of adnexal mass in premenopausal and postmenopausal women is outlined in given flowchart (Figure 2, 3).

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The Association of Obstetricians & Gynaecologists of Delhi

# 43rd Annual AOGD Conference

19 20 & 21 NOVEMBER, 2021

Organized By: VMMC & Safdarjung Hospital

*Safe Practices, Quality Services*


## *Conference Scientific Programme*

## Day 1 | Friday, 19th November 2021

### Hall A

| |
|---|
| **Labour- Newer Perspective** |
| Labour Care Guide Overview & Demonstration |
| Respectful Maternity Care |
| Reaching SDG Goal by Preventing PPH |
| **Too Small & Too Soon-The Rescue Toolbox** |
| Imaging in FGR |
| Prediction & Prevention of Preterm Labour |
| IKMC- Innovation Extended to Unstable Babies : Obstetrician & Neonatologist Viewpoints |
| **AOGD Presidential Oration** |
| Work & Worship |
| **On the Edge: Obstetric Conditions** |
| Peri-Partum Acute Kidney Injury |
| Dyspnea in Pregnancy |
| Acute Liver Failure in Obstetrics |
| Dealing with Thromboembolism in Pregnancy |

### Hall B

| |
|---|
| **Let Her be Pain Free** |
| Chronic Pelvic Pain: Overview |
| Medical Management of PID |
| Surgical Management of PID |
| **Mixed Bag** |
| Is It Time for Universal Non Invassive Pre-Implantation Genetic Testing? |
| Panel: Demystifying Mullerian Anomalies: Diagnosis to Treatment |
| **AOGD Presidential Oration** |
| Work & Worship |
| **Family Welfare** |
| Recent Advances in Contraception |
| **Panel:** Pregnancy Termination for Medical Disorders : Adressing the Dilemma |

# Day 2 | Saturday, 20th November 2021

## Hall A

| |
|---|
| **Infection in Ob/Gyn-Bundle Approach** |
| Surgical Site Infections – Prevention & Management |
| Dealing with Sepsis in Obstetrics |
| **Nurture the Special Pregnancy** |
| Pregnancy Following IVF |
| Pregnancy Following Recurrent Pregnancy Loss |
| Pregnancy After Uterine Surgery |
| **New frontiers in Obstetrics** |
| ERAS in Obstetrics-The New Frontier |
| Vaccination in Pregnancy |
| **Solving pregnancy Dilammans- Dialogue with Experts** |
| Thrombocytopenia in Pregnancy |
| Managing Gravidas with Corrected Cardiac Anomaly |
| **Pregnancy Hypertensive Disorders : Don't Let the Volcano Erupt** |
| Prediction of Pre-Eclampsia |
| Prognostic Role of Full Pier & Biomarkers |
| Neurological Complications of Pre-Eclampsia |

## Hall B

| |
|---|
| **Keeping Pace with Recent Advances** |
| Breast Screening:  Indian Guidelines |
| Ovarian Cancer-Early Diagnosis |
| **Endometrial Carcinoma- Still an Enigma** |
| **Panel:** Prevention & Progress of Endometrial Cancer |
| **Optimizing Fertility Outcome** |
| Genital Tuberculosis |
| Endometriosis |
| Cancer Survivors |
| Premature Ovarian Insufficiency |
| **Redeeming Quality of Life after Menopause** |
| **Panel** : Managing Challenging Clinical Scenarios |

# Day 3 | Sunday, 21st November 2021

## Hall A

| |
|---|
| **Decoding Fetal Medicine** |
| Preconception Screening-What & When |
| Prenatal Surgical Interventions |
| **Panel**- Dealing with Fetal Anomalies (Pyelectasis/ Ventriculomegaly) |
| **Brig Khanna Oration** |
| Bladder Pain Syndrome |
| **Gestational Diabetes -Solving the Conundrum** |
| Insulin Therapy in Pregnancy |
| Continuum of Care: Intrapartum to Postpartum |
| **Panel :** Controversies in Hyperlycemia in Pregnancy |
| **Competition Papers** |
| **Current Buzz: Let's Debate** |
| PROM Termination at 34 Weeks |
| Antenatal Corticosteroid in Late Preterm Labour |
| **Slogan Competition** |

## Hall B

| |
|---|
| **Lets Talk About Vulva** |
| Revised Vulval Carcinoma Staging-2021 - Clinical Practice Implications |
| **Panel:** Practice Essential of Vulvar Lesions- Lessons to Learn |
| **Brig Khanna Oration** |
| Bladder Pain Syndrome |
| **Urogynaecology** |
| Tips and Tricks of Vaginal Surgery: Preventing Prolapse Recurrence |
| Laser Based Devices in Urogynecology - Current Practices |
| Prolapse & Urinary Incontinence Management -Conservative Approach |
| **Panel :** Evaluating & Managing Urinary Incontinence. |
| **Competition Papers** |
| **Current Buzz: Let's Debate** |
| USG for Diagnosis of Adolescent PCOS |
| All Post-Menopausal Ovarian Cysts Need Surgery |
| **Slogan Competition** |

The Association of Obstetricians & Gynaecologists of Delhi

# 43rd Annual AOGD Conference

**19 20 21 NOVEMBER, 2021**

**Organized By: VMMC & Safdarjung Hospital**

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|---|---|---|---|
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| Workshops | | Proposed Dates |
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| FETAL INTERVENTIONS (APOLLO HOSPITAL) | ☐ | 11 - 11 - 2021 |
| STILL BIRTH PREVENTION & MANAGEMENT (LHMC) | ☐ | 12 - 11 - 2021 |
| PICSEP (FOGSI) | ☐ | 13 - 11 - 2021 |
| MEDICO-LEGAL (MAMC & LNJP HOSPITAL) | ☐ | 14 - 11 - 2021 |
| POST PARTUM HAEMORRHAGE (DDU) | ☐ | 15 - 11 - 2021 |
| HYPERANDROGENISM: EVIDENCE BASED METHODOLOGY( MAX SAKET) | ☐ | 16 - 11 - 2021 |
| LAPAROSCOPY & HYSTEROSCOPY: BASICS & BEYOND (FORTIS LAFEMME & SGRH) | ☐ | 17 - 11 - 2021 |
| 3 P'S OF CERVICAL CANCER (PROTOCOLS, PROCEDURES, PREVENTION) (SJH) | ☐ | 18 - 11 - 2021 |
| REVISITING BASIC INFERTILITY PRACTICES (SJH) | ☐ | 22 - 11 - 2021 |
| FIGHTING THE FRIGHT: NON HAEMORRHAGIC MATERNAL COLLAPSE (GTB) | ☐ | 23 - 11 - 2021 |
| UROGYNAECOLOGY - OASIS EPISIOTOMY (SGRH) | ☐ | 24 - 11 - 2021 |
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2. All cancellation received before 15th september2021 will be entitled for 75% refund of the amount paid.
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# Genetic Counselling in Gynaecological Cancers

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[1]Senior Resident, [2]Professor and Head of Unit, VMMC and Safdarjung Hospital, New Delhi

## Introduction

Cancer exists as a barrier to increasing life expectancy in every country and ranks as a leading cause of death in the world. According to estimates from the World Health Organization (WHO) in 2019, cancer is the first or second leading cause of death before the age of 70 years in 112 of 183 countries and ranks third or fourth in a further 23 countries.[1]

Now-a-days, panel testing has become a dominant means for genetic risk evaluation. In gynecological cancers, multi-gene panels are used for cancer susceptibility including BRCA1 and BRCA2 making it important for oncologists to understand the risks associated with mutations in various genes. The major focus is on epithelial ovarian cancer (OC) and endometrial cancer (EC).

Assessment of germline pathogenic variants (mutations) and their association with cancer is done by clustering genes by their penetrance (lifetime risk) for the development of the disease. The terms "high," "moderate," and "lower" penetrance provide an assessment of associated cancer risks. A relative risk (RR) of cancer greater than 4 are considered high penetrance, with RRs of 2 to 4 and less than 2 considered moderate and lower penetrance genes, respectively.

## Epithelial Ovarian Cancer

Ovarian Cancer (OC) is mostly sporadic. It is a heterogenous disease with multiple histologic subtypes, out of which, epithelial subtype compromises more than 90% of the cases. About 70% of epithelial ovarian cancer is diagnosed at stage III and IV and have a 5 year survival of 37% and 25% respectively.[2]

*Risk of Epithelial OC in the family-* Ovarian Cancer has a significant heritable component, providing opportunities for identification of women at risk and subsequent surgical risk reduction. There exists a significant risk with a RR of approximately 3 for women with family history of OC. At least 15% of women with high grade non-mucinous ovarian cancer have germline mutation in BRCA 1/BRCA2, of which 40% have no family history of breast or ovarian cancer.[3] Ten percent of the heritable component are explained by mutations in other single genes, and approximately 6% by polygenic risk represented by single nucleotide polymorphisms (SNPs) identified in genome-wide association studies (GWAS).

The genes associated with Epithelial OC have been postulated in the table below: (Table 1)[5]

**Table 1:** Genes associated with Epithelial Ovarian Cancer

| Gene | Epithelial Ovarian Cancer |
|---|---|
| ATM | Absolute risk: <3%<br>Management: risk reduction (insufficient evidence); manage as per family history<br>Strength of evidence: Strong |
| BRCA 1 | Absolute risk: 39-58%<br>Strength of evidence: Very Strong |
| BRCA 2 | Absolute risk: 13-29%<br>Strength of evidence: Very Strong |
| BRIP 1 | Absolute risk: >10%<br>Management: risk reduction – consider RRSO at 45-50years<br>Strength of evidence: Strong |
| MSH2, MSH6, MLH1, PMS2, EPCAM | Absolute risk:<br>MLH1, MSH2 - >10% (strong evidence)<br>MSH6 - ≤13% (mixed evidence)<br>EPCAM, PMS2 - <3% (limited evidence) |
| PALB2 | Absolute risk: 3-5%<br>Management: risk reduction- evidence insufficient, based on family history<br>Strength of evidence: Strong |
| RAD51C, RAD51D | Absolute risk: >10%<br>Management: risk reduction (consider RRSO at 45-50years)<br>Strength of evidence: Strong |

## BRCA 1 and BRCA 2

Mutations in BRCA 1/2 are the strongest single risk factor for the development of disease. Around 1 in 300 individuals carry BRCA 1/2 mutations in the general population and occur more frequently in some founder populations such as Ashkenazi Jewish groups. These women are at a higher risk to develop high-grade serous adenocarcinomas as opposed to mucinous tumors. Mutations in BRCA1 are associated with an OC risk in prospective studies as great as 44% by age 80 years, along with a risk of breast cancer of approximately 70%.[6] Mutations

in BRCA2 are associated with increased risks of breast (lifetime risk of up to 70%) and OC (lifetime risk of 10% to 20%), along with pancreatic cancer and high-grade prostate cancer.[7] Genetic testing and counselling thus has an increased role in these women.

## Genetic Testing

At-risk women should be offered informed pre-test counselling and genetic testing once consented. Many of the times, educating them of the consequences and emphasizing its importance becomes a necessary step. The aim of genetic testing is to help at risk individuals to:

- Understand the information regarding the genetic condition
- Understand the risk of recurrence and inheritance patterns
- Understand available options and make informed choices by customizing the information as per their personal and family situations
- Understand the adjustments they need to make as per the condition and risk

Genetic testing needs to be performed on the index patient, her siblings and daughters. It is usually performed on DNA from a blood sample or saliva or tissue biopsy. Locating the mutation is usually difficult and for high risk families one may need to first test a living relative who has already developed cancer. In nearly 20%, the mutation cannot be located in the family.

Testing is indicated in the following scenarios:[5]

- Family or personal history of epithelial ovarian cancer (including fallopian tube cancer or peritoneal cancer) at any age
- Unaffected individual with a first- or second-degree blood relative with epithelial ovarian cancer (including fallopian tube cancer or peritoneal cancer) at any age
- Individuals with any blood relative with a known pathogenic/likely pathogenic variant in a cancer susceptibility gene
- Individuals meeting the criteria below but tested negative with previous limited testing (eg, single gene and/or absent deletion duplication analysis) interested in pursuing multi-gene testing
- A mutation identified on tumor genomic testing that has clinical implications if also identified in the germline
- To aid in systemic therapy and surgical decision-making
- Individual who meets Li-Fraumeni syndrome (LFS) testing criteria or Cowden syndrome/PTEN hamartoma tumor syndrome testing criteria or Lynch syndrome
- An unaffected individual who otherwise does not meet the criteria above but has a probability >5% of a BRCA1/2 pathogenic variant based on prior probability models (eg, Tyrer-Cuzick, BRCAPro, CanRisk)

Testing **may be considered** in the following scenario (with appropriate pre-test education and access to post-test management):[5]

- An individual of Ashkenazi Jewish ancestry without additional risk factors
- Multiple primary breast cancer, first diagnosed between age group of 50 to 65 years
- An individual with 2.5 to 5% probability of BRCA1/2 pathogenic variant based on prior probability models

## Pre-test Counseling

It includes the following elements:[5]

1. Obtain a written and informed consent
2. Evaluation:
   - Individuals needs and concerns
   - Detailed family history:
     - Assessing family history; close blood relatives include first, second, and third degree relatives on each side of the family, particularly around individuals with a diagnosis of cancer
     - Types of cancer, bilaterality, age at diagnosis, subtype, and pathology report confirmation
     - Ethnicity
   - Detailed medical and surgical history including:
     - Personal cancer history (eg, age, histology, laterality)
     - Pathology reports of primary cancers and/or benign lesions (eg, breast biopsies)
     - Carcinogen exposure (eg, history of radiation therapy)
     - Reproductive history
     - Hormone or oral contraceptive use
     - History of risk-reducing surgeries
   - Focused physical examination
3. Generate a differential diagnosis and educate

the patient on inheritance patterns, penetrance, variable expressivity, and the possibility of genetic heterogeneity

4. Prepare for the possible outcomes of testing, including positive (pathogenic, likely pathogenic), true negative and uninformative negative, uncertain variants, and mosaic results
5. Discuss plan for results disclosure when appropriate, including the possibility of the patient consenting to Release of Information of test results to a close relative or spouse when results are released in case patient is deceased or incapacitated
6. Discuss possible management options if a mutation is identified (enhanced surveillance, risk-reducing agents, and risk-reducing surgery)
7. Advise about possible inherited cancer risk to relatives, options for risk assessment, testing, and management
8. Discuss cost of genetic testing
9. Provide overview of current legislation regarding genetic discrimination and the privacy of genetic information

## Post-test Counselling

It includes the following elements:[5]

- Discussion of results and associated medical risks
- Interpretation of results in context of personal and family history of cancer
- Discussion of recommended medical management options
- Discuss the importance of notifying family members and offer materials/resources for informing and testing at-risk family members.
- Discuss available resources such as high-risk clinics, disease-specific support groups, and research studies.
- Reproductive age patients –
  - advise about options for prenatal diagnosis and assisted reproduction, including pre-implantation genetic testing
  - discuss known risks, limitations, and benefits of these technologies
- Testing family members for a VUS if there is data to support discrepancy in interpretation of results

If the test comes out to be negative, individual must be counselled that there still exists a risk higher than the general population. She must be offered chemoprevention with long term combined oral contraceptives. If such a woman is postmenopausal and undergoing hysterectomy for benign indication, she must be offered risk reducing bilateral salpingo-oopherectomy in the same sitting.

If the test comes out to be positive, one may begin screening for such a woman at 30 years of age or 5 to 10 years before the earliest age of first diagnosis of ovarian cancer in her family and continue so at 6 monthly intervals using TVS (D1 to D10) and CA 125 after D5. We must recommend risk-reducing salpingo-oophorectomy (RRSO), typically between 35 and 40 years, and upon completion of childbearing. BRCA 2 pathogenic or likely pathogenic variants occur on an average of 8–10 years later than in patients with BRCA1 pathogenic/likely pathogenic variants. Hence it is reasonable to delay RRSO for management of ovarian cancer risk until age 40–45 years in patients with BRCA 2 pathogenic/likely pathogenic variants unless age at diagnosis in the family warrants earlier age for consideration of prophylaxis.

It is also important to discuss regarding the reproductive desires, extent of cancer risk, degree of protection for breast and ovarian cancer, management of menopausal symptoms, hormone replacement therapy, and related medical issues. Screening for other cancers for familial syndromes is also done e.g. Breast, skin, and pancreas. Screening of breast cancer must be done with clinical breast examination and annual mammography after 30 years of age and she may be even offered RR mastectomy. NICE also recommends that women who have a strong family history of breast cancer but who have not been diagnosed with the disease be offered 5 years of chemoprevention with Tamoxifen. With a family history of Lynch II syndrome, one may screen for endometrial and colon cancer as well.

## Endometrial Cancer

*Inheritance of endometrial cancer*- Hereditary basis for endometrial cancer (EC) is present in 10% cases and rest are sporadic. For the development of familial EC, two genetic models were described: HNPCC or Lynch II syndrome and a predisposition for endometrial cancer alone; both are inherited in an autosomal dominant fashion.

*Risk of endometrial cancer*- The lifetime risk of endometrial cancer in women with Lynch II syndrome is 32% to 60% and the lifetime risk of ovarian cancer is 10% to 12%. It is also associated

with Cowden syndrome. EC risk has also been found to be increased with POLE, POLD1, RAD51C, RAD51D, and BRIP1 mutations but the data are too limited to provide any estimates of risk.

Lynch Syndrome has the strongest association with EC risk. Although germline mutations in MMR genes are found in less than 5% of individuals with EC, but have significant implications. The lifetime risk of EC by age 70 years as approximately 46% to 54% for MLH1 mutations, 21% to 51% for MSH2 mutations, 16% to 49% for MSH6 mutations, and 13% to 24% for PMS2 mutations.[10]

In individuals with documented Lynch syndrome, screening for colon cancer must be done using periodic colonoscopy every 1-2 years, beginning at 20 to 25years or 2 to 5 years before the earliest colon cancer diagnosis in the family, whichever is earlier. Alongside, they must have endometrial biopsy every 1 to 2 years starting at age 30 – 35years and after childbearing is completed they must undergo prophylactic hysterectomy and BSO discussion regarding which must be done in their early to mid-40s.

In 2006, a European workshop of 21 experts (the Mallorca group) recommended a surveillance strategy for patients with HNPCC or Lynch II syndrome which comprises of annual pelvic examination, transvaginal ultrasound, and endometrial biopsy beginning at 30 to 35 years of age.[9] But it is unknown whether these interventions are cost-effective or will impact mortality from endometrial or ovarian cancer in patients with Lynch II syndrome.

## Cervical Cancer

Minimal deviation adenocarcinoma is a rare entity which accounts for 1-3% of all cervical adenocarcinomas and is related with sporadic STK11 (serine/threonine kinase 11) mutations. It can be associated with Peutz-Jeghers syndrome. Due to its rarity, recommendations have not been formulated for the same.

## Gestational Trophoblastic Neoplasia

Women with recurrent molar pregnancy in the family are suggestive of dysregulation of normal parental imprinting of genes, with loss of maternally transcribes genes. Familial recurrent hyatidiform molar pregnancy is a rare occurrence which is characterized by recurrent complete hyatidiform mole of biparental origin. Such couples can undergo genetic mapping for NLRP7 (present on chromosome 19q13.4) and KHDC3L. If either mutation is detected, the couple must be counselled and oocyte donation must be proposed as an option in order to maximize the woman's chances of having a normal pregnancy. Another alternative would be surrogacy. Such couples need counselling and emotional support.

The optimal approaches to genetic testing are evolving. One may either recommend simultaneous germline and somatic sequencing, or somatic testing with reflex to germline testing if a pathogenic/likely pathogenic variant is found. For the latter approach, it is important for the individual to undergo germline testing if a somatic mutation is found in order to understand future cancer risks and also to provide information to family members. But if a somatic mutation is not found, consideration to germline testing must be still given because large genomic rearrangements can be missed with many of the current somatic sequencing platforms. However, many of the women undergoing genetic testing fail to receive in- person genetic counselling due to lack of resources. The role of newer models using telecommunication and the internet are being developed to allow in- person counselling of all individuals.

## Advantages

Genetic counselling and testing provides an advantage of knowing the inheritance pattern and cancer risks for the individual and their family members. This helps to plan a follow up, timely recognition and timely life-saving intervention. If an individual with ovarian cancer has a germline mutation, it might indicate an increased sensitivity to PARP (poly (ADP) –ribose polymerase) inhibitors and/or platinum compounds and help in improving survival.

## Limitations

One must also be aware regarding the limitations of multigene panels which include detection of "intermediate" penetrant (moderate-risk) genes but there are limited data on the degree of cancer risk, no clear guidelines on risk management for carriers of pathogenic/likely pathogenic variants, and not all genes included on available multi-gene tests are necessarily clinically actionable. Also the information from testing for moderate penetrance genes does not change risk management compared to that based on family history alone in many. There is also

an increased likelihood of finding VUS, mosaicism, and clonal hematopoiesis of indeterminate potential (CHIP), pathogenic/likely pathogenic variants without clear clinical significance. The affordability with respect to cost of the test is also an issue.

## Conclusion

The identification of mutations is increasing with multigene panel testing for cancer susceptibility in genes (other than BRCA1 and BRCA2), and an expanding number of genes have been found to be associated with OC although the magnitude of OC risk changes across genes. Any individual with ovarian tumor must be offered counselling and genetic testing which has both preventive and therapeutic advantage. In the future, the application of genomics in medicine is increasing and the costs are falling, hence its incorporation into routine care becomes important. Every gynaecologist must be aware and trained for counselling with regards to genetic testing in such women and making them understand its clinical application.

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# The Role of Vulval Scrape Cytology and Colposcopy in Evaluation of Chronic Vulval Symptoms

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## Abstract

**Background:** Chronic vulvar symptoms cause excruciating discomfort in women who often delay seeking medical attention. Many practitioners feel diagnostically challenged particularly by chronic form of vulval disease as there is no diagnostic algorithm for such problems. **Objective:** To assess the role of vulval cytology and colposcopy in evaluation of chronic vulval symptoms. **Setting:** Department of Gynaecology and Dermatology of a tertiary care hospital in a tertiary care hospital. **Study Design:** Cross-Sectional Study. **Methods:** We studied 100 women presenting to the gynaecology or dermatology clinic of Safdarjung Hospital with chronic vulvar symptoms (pruritus, pain or lesion on the vulva) who underwent vulval scrape cytology, colposcopy & directed biopsy. The sensitivity and specificity of the tests was calculated taking histopathology as the gold standard. **Statistical Analysis:** Mac Nemar's test was used to compare various diagnostic methods. **Results and Conclusions:** The overall sensitivity and specificity for detecting vulvar lesions was 58.44% and 13.04% with Cytology and 77.92 % and 17.39 % with colposcopy respectively. The Positive Predictive Value was 69.23% for cytology and 75.95 % for Colposcopy. Vulval Colposcopy had a 100% negative predictive value in excluding a neoplastic lesion. **Conclusion:** Vulval cytology & colposcopy have a high negative predictive value and provide reassurance in the absence of disease.

**Key Words:** Chronic Vulval Conditions, Pruritus, Cytology, Colposcopy

## Introduction

Vulvo-vaginal symptoms are among the most common reasons for women seeking health care.[1,2] Chronic vulval conditions (pruritus, vulvodynia and vulval lesions) are common presentation in gynaecological clinics; the commonest being pruritus and vulvodynia. Despite this, gynaecologists feel diagnostically challenged when presented with women with these symptoms, and feel that colposcopy and biopsy alone can make a diagnosis.

Vulval scrape cytology, though used less often, is an effective and easy diagnostic technique for evaluation of chronic vulval symptoms.[3] Colposcopy of the vulva was first described by Coppleson & Pixely in 1976; however not often used by gynaecologists for evaluation of the vulva and also not readily available at all centres.[4] Vulvar cancers account for 1-3% of all cancers reported in India every year. However, there is no organized screening program and majority of Indian women lack awareness and access to disease prevention and treatment facilities. Chronic vulvar symptoms include pruritus, pain and changes in skin colour and texture. Community-based surveys indicate that about one-fifth of women have significant vulvar symptoms. The most important step in evaluating chronic vulvar problems is a good history and careful clinical examination. Various diagnostic aids like vulval scrape cytology and colposcopy have been studied and are adjuncts to biopsy in diagnosis. The aim of our study was to assess the role of vulval cytology and colposcopy in evaluation of chronic vulval symptoms; the gold standard being vulval biopsy and histopathology.

## Material and Methods

Study Design: Cross-Sectional Study

Setting: Department of Gynecology and Dermatology Vardhmaan Mahaveer Medical College and Safdarjung Hospital, New Delhi.

Method: Institutional Ethical Board clearance was taken and 100 sexually active women attending our gynaecology or dermatology clinic with complaints of vulvar pruritus, vulvodynia or lesion on the vulva of ≥ 3 months duration were recruited into our study after taking informed signed consent for research.

A detailed history was taken from each woman, including details of vulvar hygiene, usage of deodorants and gels on the vulva, followed by a

gynecological examination. Women who were not sexually active, were symptomatic for <3months, had generalised symptoms, or vaginal discharge were excluded from the study.

A vulval scrape cytology was taken using a no 15 blade as described by Dennerstein et al[3] after moistening the vulva with normal saline. The scrape was taken from the mucocutaneous junction and additionally from any lesion found on the vulva. The slides were them immediately fixed with cytospray (95% ethyl alcohol) and processed as usual for Papanicolaou smears. The smears were then interpreted as per Bethesda terminology.[5]

This was followed by colposcopy after applying 5% acetic acid. Colposcopic findings were described using Coppleson & Pixley's classification.[4] Vulvar biopsy was taken from suspicious areas; histopathological findings were classified as per ISSVD Classification 2006.[6]

Statistical Analysis: The sensitivity, specificity, positive predictive value, negative predicative value and accuracy of examination with cytology and colposcopy were calculated taking histopathology as gold standard both for benign and malignant lesions. Mac nemar's test was used to compare various diagnostic methods.

## Results

We had 100 women who presented with chronic vulval symptoms, the common symptoms were pruritus vulvae in 92, vulval lesion in 20 and vulvodynia in 11. The vulval scrape cytology was normal in 39, reactive changes in 23, benign vulvar changes – vulvitis in 35 and benign vulvar changes – candidiasis in 3 patients. The colposcopic findings were normal in 21, white lesion in 8, acetowhite lesions in 70 and black pigmentation in 1 patient. The findings on cytology and colposcopy are summarized in table 1.

**Table 1:** Findings on Vulval Scrape Cytology & Colposcopy

| **Distribution of patients (n=100) by cytology of vulva** | |
|---|---|
| Normal | 39 |
| Reactive changes | 23 |
| Benign vulvar changes- vulvitis | 35 |
| Benign vulvar changes- candidiasis | 3 |
| **Distribution of patients(n=100) by colposcopy findings** | |
| Normal | 21 |
| White Lesion | 8 |
| Acetowhite Lesions | 70 |
| Black Pigmentation | 1 |

Bethesda classification[6] was used to classify the vulval smears. The histopathology was reported as per ISSVD (The International Society for the Study of Vulvovaginal Disease) 2006 classification, the histopathological diagnosis is as given in table 2. The most common histopathological diagnosis was Nonneoplastic epithelial disorders (NNED) – squamous cell hyperplasia in 52% patients. The other histopathological fidings were NNED – Lichen Sclerosis et atrophicus (LSEA) in 6%, NNED – other dermatoses in 6%, Squamous VIN 1 in 3%, Squamous VIN 2 in 1%, Squamous VIN 3 in 1%, Non-squamous VIN – Pagets in 1%, Invasive carcinoma-Squamous cell carcinoma in 3%, Melanocytic tumours in 1%, Epithelial tumours- glandular type in 1%, Soft tissue tumours in 2% and normal in 23% patients.

**Table 2:** Distribution of patients by histopathology examination of vulva

| **HPE of Vulva (ISSVD Classification)** | **No. of patients** | **Percent** |
|---|---|---|
| NNED- Squamous Cell Hyperplasia | 52 | 52.0 |
| NNED- LSEA | 6 | 6.0 |
| NNED- Other- Dermatoses | 6 | 6.0 |
| Squamous VIN 1 | 3 | 3.0 |
| Squamous VIN 2 | 1 | 1.0 |
| Squamous VIN 3(Severe Dysplasia) | 1 | 1.0 |
| Non Squamous VIN-Pagets | 1 | 1.0 |
| Invasive Carcinoma -SCC | 3 | 3.0 |
| Melanocytic Tumours | 1 | 1.0 |
| Epithelial Tumours- Glandular Type | 1 | 1.0 |
| Soft Tissue Tumours | 2 | 2.0 |
| Normal | 23 | 23.0 |

Vulval scrape cytology had a sensitivity of 58.44% (95% CI 46.64%-69.57%) and specificity of 13.04% (95% CI 2.78-33.59%). The sensitivity for detecting neoplastic lesions by cytology was 100% (95% CI 71.51%-100%) and specificity was 13.04% (95% CI 2.78-33.59%) respectively.

Colposcopy had a sensitivity of 74.24% (95% CI 61.99%-84.22%) and specificity of 17.39% (95% CI 4.95%-38.78%) for detecting any vulvar lesion; however it was 100% sensitive with a specificity of only 17.39% (95% CI 4.95%-38.78%) for detecting neoplastic lesions. The sensitivity, specificity, positive and negative predictive values of vulval

**Table 3:** Comparison of Diagnostic Tests: Normal vs any abnormality

| | Sensitivity | Specificity | PPV | NPV |
|---|---|---|---|---|
| Cytology | 58.44% | 13.04% | 69.23% | 8.57% |
| 95% CI | 46.64% to 69.57% | 2.78% to 33.59% | 56.55% to 80.09% | 1.80% to 23.06% |
| Colposcopy | 77.92% | 17.39% | 75.95% | 19.05% |
| 95% CI | 67.02% to 86.58% | 4.95% to 38.78% | 65.02% to 84.86% | 5.45% to 41.91% |

**Table 4:** Comparison of Diagnostic Tests for Normal vs neoplastic abnormality

| | | | | |
|---|---|---|---|---|
| Cytology | 100.00% | 13.04% | 35.48% | 100.00% |
| 95% CI | 71.51% to 100.00% | 2.78% to 33.59% | 19.23% to 54.63% | 29.24% to 100.00% |
| Colposcopy | 100.00% | 17.39% | 36.67% | 100.00% |
| 95% CI | 71.51% to 100.00% | 4.95% to 38.78% | 19.93% to 56.14% | 39.76% to 100.00% |

scrape cytology and colposcopy is given in table 3 & 4.

## Discussion

Chronic vulvar lesions are a diagnostic enigma. Gynaecologists who are not trained in colposcopy often feel handicapped in evaluating these women as identifying the ideal diagnostic method is a challenge. Our study was carried out with the aim of assessing the role of vulval scrape cytology and colposcopy in evaluation of chronic vulval symptoms. In our study, vulvar scrape cytology had 100% sensitivity for detecting neoplastic lesions; although specificity was low. However, it had a 100% negative predictive value which could be very reassuring. Jimenez A[5] studied 563 patients and used scraping technique for obtaining vulvar smears and reported sensitivity and specificity of 97.7% and 98.87% respectively for benign lesions and 98.21% and 94.82% respectively for malignant lesions. Bae e al[7] on a retrospective study of 400 patients who had vulval smears collected by scraping method also found sensitivity and specificity of vulvar cytology to be 32.8% and 88.62% respectively. Smaller studies by Wendy likes[8] (n=48) and Van den Einden[9] (n=23) also reported a high correlation of 91% and sensitivity of 100%.

Colposcopic changes in vulval disease were first described by Coppleson et al in 1976. Since then, colposcopy has been used for detection of vulvar disease. Santoso JT, Likes W[10] on their study on 344 patients with vulval symptoms found the sensitivity, specificity, positive and negative predictive value of Colposcopy for detection of high grade VIN was 97%, 40%, 37 & 98% respectively. We found an overall sensitivity of colposcopy to be 77.9% (95% CI 67.02-86.58%). Though the specificity of colposcopy is low at 17.39% but it has a high negative predictive value. Therefore, a normal colposcopy in the presence of chronic vulvar symptoms would be very reassuring.

In conclusion, when facilities for colposcopy are not available; vulval scrape cytology can also detect any dysplastic cells. Colposcopy & biopsy are the gold standard, their low specificity is offset by a high negative predictive value. A negative vulval scrape cytology and colposcopy can be very reassuring to the woman distressed with chronic vulval symptoms.

## Conclusion

In our study, the commonest chronic vulvar symptom was pruritus and the most common histopathological abnormality was non- neoplastic epithelial disorders- squamous cell hyperplasia. When facilities for colposcopy are not available; vulval scrape cytology can be taken which can detect any dysplastic cells since it is an easy and effective way of evaluating chronic vulval symptoms. Colposcopy had overall sensitivity of 77.92% and specificity of 17.39%; however it could detect all of the malignant lesions. Colposcopy & biopsy are gold standard tests; however, their low specificity is offset by a high negative predictive value. From our study, we concluded that vulval scrape cytology and colposcopy have high negative predictive value and provide reassurance in absence of disease.

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# Evaluation of Inflammatory Pap smear for Cervical Intraepithelial Lesion

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## Abstract

**Objectives:** To detect epithelial cell abnormalities in women with persistent inflammation on pap smear. **Methods:** This cross sectional study was conducted in the Department of Obstetrics and Gynecology and Pathology, of a tertiary care hospital. To achieve a sample size of 80 calculated by assuming a medium effect size (0.5) with 80% power of study and two sided alpha of 5%, 500 asymptomatic, sexually active women, 21-65 years were screened. Women with active genital tract infection, frank malignancy, pregnancy, IUCD, diagnosed cervical intraepithelial neoplasia (CIN), multiple sexual partners, or history of diabetes were excluded from the study. Women with a Pap smear report suggestive of inflammation were included in the study. Both the partners were treated with antibiotics. Follow up visit was scheduled after 6 weeks and a repeat Pap smear was taken and VIA was done at the same visit. In VIA positive cases, colposcopy and if required a directed biopsy was done at the same sitting. VIA negative women who showed persistent inflammation on repeat pap smear were also subjected to colposcopy and guided biopsy if indicated. Women with normal Pap smear report and VIA negative were followed up with routine screening. Statistical analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0. **Results:** Out of 500 women, 400 (80%) had inflammation on initial Pap smear. VIA was positive in 20/400 women, colposcopy directed cervical biopsy was suggestive of CIN in 16/20 (80%) and chronic cervicitis in 4 women. CIN 1, CIN 2 and CIN 3 were present in 10, 5 and 1 women, respectively. Second Pap smear showed persistent inflammatory smear in 79 women. Out of 79 women with persistent inflammation, 59 VIA negative women, 17 (28.81%) had abnormal findings on colposcopy done at 2nd visit and CIN was diagnosed in 16 (94%) women. **Conclusion:** Women with inflammatory Pap smear should be further evaluated to rule out associated Cervical Intraepithelial Neoplasia.

**Key Words:** Inflammatory Pap Smear, VIA, Colposcopy, Cervical Intraepithelial Lesion, CIN

## Introduction

Pap smear is the standard test for screening of cervical precancerous lesions which detects abnormal cervical epithelial cells harboring premalignant changes which can be treated at early stages to prevent invasive cervical cancer. The reported incidence of inflammation on Pap smear is very high in various studies.[1-4] Recent studies in India have reported a similar high prevalence of inflammation on Pap smear to be 30-40%.[5-6] Chronic inflammation, either specific or non-specific, has been shown to be associated with malignancy and is thought to be one of the factors responsible for carcinogenesis. Persistent microbial infection in and around epithelial cells results in a chronic inflammatory state resulting in a state of increased cellular turnover which may undergo metaplastic and dysplastic changes and progress to neoplasia. This has been postulated to cytokine and free radical mediated damages which cause reactive cellular hyperproliferation promoting further mutations.[7] It is well documented that due to the low sensitivity and high false negative rate, there is a possibility that an inflammatory Pap smear may miss cervical premalignant changes.

Women with persistent inflammation on Pap smear require further evaluation & treatment. Management of women with persistent inflammatory changes without atypia is not well defined, as the degree of association between dysplastic changes and cervical intra epithelial lesions (CIN) is variable. The cervical screening algorithm for benign cellular changes recommends treatment of infection and a repeat Pap smear in 4 to 6week time.[8-11] Persistent inflammatory Pap smear warrants colposcopy. Since the incidence of inflammation on Pap smear is very high, it may not be practical to subject all women with persistent inflammatory smear, to colposcopy. A cheaper method of evaluation like visual inspection after acetic acid application (VIA) can be considered.

This study was planned to find out epithelial cell abnormalities in women with persistent inflammatory smear.

## Materials and Methods

This cross sectional study was conducted between May 2017 to January 2018 in the department of Obstetrics and Gynecology and Pathology, at a tertiary care hospital in New Delhi, India. The study was approved by the Ethics Committee of the Institute. A written informed consent was obtained from all participants of the study.

Sexually active asymptomatic women between 21-65 years of age were included in the study. Women with active cervical infection, vaginitis, pelvic inflammatory disease, frank malignant lesion on cervix, pregnancy, IUCD users, previous history of CIN and treatment, multiple sexual partners or history of diabetes were excluded from the study.

The cytological criteria for inflammation was based on the nuclear abnormalities such as variation in nuclear size, enlargement, binucleation, dyskaryosis, pyknosis, karyorrhexis and presence of polymorphs in the smear in numbers adequate to obscure the epithelial cells. Cytoplasmic irregularity in the form of altered staining reaction, vacuolation and increased granularity was also considered abnormal. The grading of the inflammatory changes was done as minimal, mild, moderate and severe depending upon the degree of nuclear and cytoplasmic changes and polymorphonuclear cellular infiltration.

A total of 500 women were screened with Pap smear to achieve a sample size of 80, calculated by assuming a medium effect size (0.5) with 80% power of study and two sided alpha of 5%. Women with a Pap smear report suggestive of inflammation were included in the study. Both the partners were treated. Women received oral Doxycycline (100 mg twice a day) and oral Metronidazole (500 mg twice a day) for two weeks, along with a single dose of oral Cefixime (400mg) and husband/partner received a single dose of oral Azithromycin (1 gram) and oral Cefixime (400 mg) as per the national guidelines. Barrier contraception was advised for the same duration.

After this course of antibiotics, women were called six weeks later and a repeat Pap smear was taken followed by naked eye examination of cervix after acetic acid application (VIA) at the same visit. In VIA positive cases, colposcopy was done at the same sitting, followed by directed biopsy if required. Pap smear report was evaluated later. Patients with persistent inflammation, even if VIA negative, were subjected to colposcopy and guided biopsy. Women with normal Pap smear report and VIA negative were followed up with routine screening.

The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0. Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean ± SD and median. Normality of data was tested by Kolmogorov-Smirnov test. If the normality was rejected then non parametric test was used. Quantitative variables were compared using Unpaired t-test/Mann-Whitney Test. Qualitative variables were compared using Chi-Square test /Fisher's exact test. A p-value of $<0.05$ was considered statistically significant.

## Results

Among the 500 women screened, 400 women (80%) had an initial Pap smear report suggesting inflammation. VIA was positive in 20/400 women, colposcopy directed cervical biopsy was suggestive of CIN in 16/20 (80%) and chronic cervicitis in 4 women. CIN 1, CIN 2 and CIN 3 were present in 10, 5 and 1 women, respectively.

Out of 79 women with persistent inflammation, 59 VIA negative women, 17 (28.81%) had abnormal findings on colposcopy done at 2$^{nd}$ visit and CIN was diagnosed in 16 (94%) women.

On further evaluation 6 weeks after antibiotics with second Pap smear, a total of 79 women were found to have persistent inflammatory smear (Table 1).

**Table 1:** Women with positive findings on Pap smear and VIA

| VIA Paps smear | Positive | Negative | Total |
|---|---|---|---|
| Persistent inflammation | 20 | 59 | 79 |
| No inflammatory changes | 0 | 321 | 321 |
| Total | 20 | 380 | 400 |

Among the women with persistent inflammatory smear the mean age was 39.65±10.0 years and mean parity was 2. Majority of the women (87.5%) were literate and 58% were from urban areas. The most common presenting complain was pain in the lower abdomen (41.25%), followed by AUB (17.5%) and urinary complaints (10%).

In view of persistent inflammatory Pap smear these women underwent colposcopy. On colposcopy, 17(21.25%) cases had abnormal findings and were subjected to biopsy. Histopathology examination of cervical biopsy showed intraepithelial neoplasia in 16(94%) women - CIN1 in 12 cases, CIN 2 in 3 cases & CIN 3 in 1 case (Table 2).

**Table 2:** Histopathology in Colposcopy Positive Cases

| Histopathology | Colposcopy positive | | Total |
|---|---|---|---|
| | VIA+ | Persistent inflammatory Paps smear | |
| Squamous metaplasia | 0 | 1 | 1 |
| Chronic cervicitis | 4 | 0 | 4 |
| CIN 1 | 10 | 12 | 22 |
| CIN 2 | 5 | 3 | 8 |
| CIN 3 | 1 | 1 | 2 |

## Discussion

Pap smear has been proven useful for widespread screening for cancer cervix and has resulted in marked reduction in cervical cancer mortality owing to the relatively long pre-invasive phase of this neoplasm, the easy accessibility of uterine cervix for examination and availability of technique to process the cervical smear.[12,13,14] There is a concern among clinicians regarding persistent inflammatory smear as it causes a cellular microenvironment of chronic inflammation which predisposes to metaplastic and dysplastic changes in the cervical epithelium.[7]

Clear cut guidelines for the management of inflammatory smears are scanty.[8-11] The commonly followed protocol is to treat the woman with antibiotics and repeat the smear after 4-6 weeks. This conservative approach causes regression of inflammation in majority of the cases.

In a study by Brown et al., CIN 3 was present in 30% cases where persistent inflammation was present on Pap smear.[15] In our study, 40% women with persistent inflammation on Pap had various grades of CIN emphasizing the fact that inflammatory smear should be adequately followed up as per the protocol of the institution, so that no cases of preinvasive and invasive cervical cancer are missed.

Should only one inflammatory Pap smear concern the clinician? This issue was studied to find the incidence of dysplasia in single inflammatory smear.[16] In this study a total of 257 women underwent Pap smear and 207 were found to have inflammatory changes. These women were subjected to colposcopy and biopsy. Eleven cases of intraepithelial neoplasia were detected. This study evaluated the result of single smear report only and did not consider the changes after antibiotic use.

A second part of the same study evaluated the role of Pap smear after a brief course of antibiotics.[17] The smear was repeated after 3 months. They reported that inflammation on Pap smear persisted in 79% cases, regressed in 12% cases and progressed to CIN in 8% cases. In our study, 33.75% had persistent inflammation and 52.5% had regression. It was concluded that one particular organism could not be implicated and hence adequate treatment was not possible. The inflammation could either be a result of underlying viral infection or reactive changes in the mucosa.

A large population based study investigated use of two smears taken 10-12 weeks apart. The first inflammatory smear was treated with a course of antibiotics while the second inflammatory smear was followed up with colposcopy and guided biopsy.[18] The incidence of persistent inflammatory smear was 14.2% and degree of dysplasia was 22.7%. The aim of the study was to determine the incidence of premalignant lesion in the background of inflammation of cervix despite treatment. One-fifth of the women with inflammation alone had underlying dysplasia thereby ascertaining that the inflammatory cellular changes should not be considered as a normal variant especially when it is persistent following adequate therapy, and require further investigation. In our study 16% women had persistent inflammation and 40% had cervical intraepithelial neoplasia.

A study was conducted in the Indian subcontinent by Bhutia et al in 420 women where inflammatory smear was followed up with a course of antibiotics for 8-14 days and second smear was taken after 6-12 weeks.[19] They reported the rate inflammatory smear as 24.3% and of persistent inflammation to be 8.6%. Women with persistent inflammation on second smear were subjected to colposcopy and guided biopsy. Among them 16.67% (30) women had CIN.

Dasari et al studied the findings in 150 women. The first report of inflammation was followed up with antibiotic course for 7-14 days and a repeat smear was taken after 2 weeks.[20] Persistent inflammation was followed with colposcopy and guided biopsy. The incidence of pre-malignant lesions was 20.9% and CIN 2/3 and carcinoma in situ together contributed to 6.9% of the cases.

From the various studies (Table 3) mentioned above it seems that the interval between the initial Pap and repeat evaluation is not significant, but it is essential to treat the inflammation adequately and retest to ensure that no case of CIN are missed.

**Table 3:** Comparing our results with other studies

| Study | No. of women Screened | No. of pap smear | Antibiotic use | Interval between pap smear | Result of 1st smear | Result of 2nd smear | Colposcopy | HPE (CIN) |
|---|---|---|---|---|---|---|---|---|
| **Brown[15] 1985** | 241 | 2 | Triple sulpha cream for 10-21 days | 6-8 wks | 104 (43.2%) | 20 (8.3%) | 20 | 14 (5.8%) |
| **Seckin[18] 1997** | 2798 | 2 | According to culture report | 2-12 wks | 397 (14.1%) | 238 (8.5%) | 224 | 18 (0.7%) |
| **Singh [17] 1998** | 257 | 2 | According to culture report | Follow up over 2 years | 206 (80.2%) | 163 (63.4%) | 163 | 90 (35%) (including HPV ass changes) |
| **Dasari [20] 2010** | 150 | 2 | Doxy+Metro for 2 wks Clotrimazole Pessary for 6 days | 2 weeks | 150 | 136 (90.7%) | 136 | 29 (19.3%) |
| **Bhutia [19] 2011** | 420 | 2 | Doxy+Metro for 2 wks Clotrimazole Pessary for 8 days | 6-12 weeks | 102 (24.3%) | 36 (8.5%) | 16 | 5 (1.2%) |
| **Our Study 2019** | 500 | 2 | Doxy+Metro for 2 wks | 6 weeks | 400 (80%) | 79 (16%) | 79 | 32 (6.4%) |

Our study also evaluated the role of VIA in the follow up of inflammatory smear. Our results cannot be compared as there are no similar studies. In our study, 5% women were VIA positive. These women were investigated immediately with colposcopy and guided biopsy following the VIA positive result and 4% had histopathology proven CIN. Considering the poor rate of follow up and the logistical restrictions in repeating Pap smear, VIA can be considered as a follow up method, as it is a cheap, easily available and reproducible, especially in low resource settings.

## Conclusion

Inflammatory Pap smear should be repeated as persistent inflammation may be associated with intraepithelial neoplastic changes in cervical mucosa. For women with persistent inflammatory pap smear, a policy for adequate antibiotic treatment and duration of follow up must be decided. VIA should be considered as an adjunct to Pap smear to provide early treatment.

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# Journal Scan

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## NRG Oncology/RTOG Consensus Guidelines for Delineation of Clinical Target Volume for Intensity Modulated Pelvic Radiation Therapy in Postoperative Treatment of Endometrial and Cervical Cancer: An Update

***Small W Jr, Bosch WR, Harkenrider MM, Strauss JB, Abu-Rustum N, Albuquerque KV, Beriwal S, Creutzberg CL, Eifel PJ, Erickson BA, Fyles AW, Hentz CL, Jhingran A, Klopp AH, Kunos CA, Mell LK, Portelance L, Powell ME, Viswanathan AN, Yacoub JH, Yashar CM, Winter KA, Gaffney DK***

*Int J Radiat Oncol Biol Phys. 2021 Feb 1;109(2):413-424.*

**Purpose:** Accurate target definition is critical for the appropriate application of radiation therapy. In 2008, the Radiation Therapy Oncology Group (RTOG) published an international collaborative atlas to define the clinical target volume (CTV) for intensity modulated pelvic radiation therapy in the postoperative treatment of endometrial and cervical cancer. The current project is an updated consensus of CTV definitions, with removal of all references to bony landmarks and inclusion of the para-aortic and inferior obturator nodal regions.

**Methods and Materials:** An international consensus guideline working group discussed modifications of the current atlas and areas of controversy. A document was prepared to assist in contouring definitions. A sample case abdominopelvic computed tomographic image was made available, on which experts contoured targets. Targets were analyzed for consistency of delineation using an expectation-maximization algorithm for simultaneous truth and performance level estimation with kappa statistics as a measure of agreement between observers.

**Results:** Sixteen participants provided 13 sets of contours. Participants were asked to provide separate contours of the following areas: vaginal cuff, obturator, internal iliac, external iliac, presacral, common iliac, and para-aortic regions. There was substantial agreement for the common iliac region (sensitivity 0.71, specificity 0.981, kappa 0.64), moderate agreement in the external iliac, para-aortic, internal iliac and vaginal cuff regions (sensitivity 0.66, 0.74, 0.62, 0.59; specificity 0.989, 0.966, 0.986, 0.976; kappa 0.60, 0.58, 0.52, 0.47, respectively), and fair agreement in the presacral and obturator regions (sensitivity 0.55, 0.35; specificity 0.986, 0.988; kappa 0.36, 0.21, respectively). A 95% agreement contour was smoothed and a final contour atlas was produced according to consensus.

**Conclusions:** Agreement among the participants was most consistent in the common iliac region and least in the presacral and obturator nodal regions. The consensus volumes formed the basis of the updated NRG/RTOG Oncology postoperative atlas. Continued patterns of recurrence research are encouraged to refine these volumes.

## Updates and New Options in Advanced Epithelial Ovarian Cancer Treatment

***Kurnit KC, Fleming GF, Lengyel E***

*Obstet Gynecol. 2021 Jan 1;137(1):108-121.*

The medical and surgical treatment strategies for women with epithelial ovarian cancer continue to evolve. In the past several years, there has been significant progress backed by landmark clinical trials. Although primary epithelial ovarian cancer is still treated with a combination of surgery and systemic therapy, more complex surgical procedures and novel therapeutics have emerged as standard of care. Cytotoxic chemotherapy and maximal surgical effort remain mainstays, but targeted therapies are becoming more widespread and new data have called into question the role of surgery for women with recurrent disease. Poly ADP-ribose polymerase inhibitors have improved progression-free survival outcomes in both the frontline and recurrent settings, and their use has become increasingly widespread. The recent creation of treatment categories based on genetic changes reinforces the recommendation that all women with epithelial ovarian cancer have germline genetic testing, and new biomarker-driven drug approvals indicate that

women may benefit from somatic molecular testing as well. To continue to identify novel strategies, however, enrollment on clinical trials remains of the utmost importance. With the evolving data on surgical approaches, targeted therapies such as antiangiogenics and poly ADP-ribose polymerase inhibitors, and the new therapeutic agents and combinations in development, we hope that advanced epithelial ovarian cancer will eventually transition from an almost universally fatal disease to one that can increasingly be cured.

## Radiological Review of Prior Screening Mammograms of screen - detected breast cancer

***Hovda T, Tsuruda K, Hoff SR, Sahlberg KK, Hofvind S***

*Eur Radiol. 2021 Apr;31(4):2568-2579.*

**Objective:** To perform a radiological review of mammograms from prior screening and diagnosis of screen-detected breast cancer in BreastScreen Norway, a population-based screening program.

**Methods:** We performed a consensus-based informed review of mammograms from prior screening and diagnosis for screen-detected breast cancers. Mammographic density and findings on screening and diagnostic mammograms were classified according to the Breast Imaging-Reporting and Data System®. Cases were classified based on visible findings on prior screening mammograms as true (no findings), missed (obvious findings), minimal signs (minor/non-specific findings), or occult (no findings at diagnosis). Histopathologic tumor characteristics were extracted from the Cancer Registry of Norway. The Bonferroni correction was used to adjust for multiple testing; $p < 0.001$ was considered statistically significant.

**Results:** The study included mammograms for 1225 women with screen-detected breast cancer. Mean age was 62 years ± 5 (SD); 46% (567/1225) were classified as true, 22% (266/1225) as missed, and 32% (392/1225) as minimal signs. No difference in mammographic density was observed between the classification categories. At diagnosis, 59% (336/567) of true and 70% (185/266) of missed cancers were classified as masses ($p = 0.004$). The percentage of histological grade 3 cancers was higher for true (30% (138/469)) than for missed (14% (33/234)) cancers ($p < 0.001$). Estrogen receptor positivity was observed in 86% (387/469) of true and 95% (215/234) of missed ($p < 0.001$) cancers.

**Conclusions:** We classified 22% of the screen-detected cancers as missed based on a review of prior screening mammograms with diagnostic images available. One main goal of the study was quality improvement of radiologists' performance and the program. Visible findings on prior screening mammograms were not necessarily indicative of screening failure.

**Key Points:** After a consensus-based informed review, 46% of screen-detected breast cancers were classified as true, 22% as missed, and 32% as minimal signs. Less favorable prognostic and predictive tumor characteristics were observed in true screen-detected breast cancer compared with missed. The most frequent mammographic finding for all classification categories at the time of diagnosis was mass, while the most frequent mammographic finding on prior screening mammograms was a mass for missed cancers and asymmetry for minimal signs.

## Niraparib Maintenance Therapy in Patients with Platinum-sensitive Recurrent Ovarian Cancer using an Individualized Starting Dose (NORA): A randomized, double-blind, placebo-controlled phase III trial

***Wu XH, Zhu JQ, Yin RT, Yang JX, Liu JH, Wang J, et al.***

*Ann Oncol. 2021 Apr;32(4):512-521.*

**Background:** This study evaluated maintenance treatment with niraparib, a potent inhibitor of poly(ADP-ribose) polymerase 1/2, in patients with platinum-sensitive recurrent ovarian cancer.

**Patients and Methods:** In this phase III, double-blind, placebo-controlled study conducted at 30 centers in China, adults with platinum-sensitive recurrent ovarian cancer who had responded to their most recent platinum-containing chemotherapy were randomized 2 : 1 to receive oral niraparib (300 mg/day) or matched placebo until disease progression or unacceptable toxicity (NCT03705156). Following a protocol amendment, patients with a bodyweight <77 kg or a platelet count $<150 \times 10^3$/μl received 200 mg/day, and all other patients 300 mg/day, as an individualized starting dose (ISD). Randomization was carried out by an interactive web response

system and stratified by BRCA mutation, time to recurrence following penultimate chemotherapy, and response to most recent chemotherapy. The primary endpoint was progression-free survival (PFS) assessed by blinded independent central review.

**Results:** Between 26 September 2017 and 2 February 2019, 265 patients were randomized to receive niraparib (n = 177) or placebo (n = 88); 249 patients received an ISD (300 mg, n = 14; 200 mg, n = 235) as per protocol. In the intention-to-treat population, median PFS was significantly longer for patients receiving niraparib versus placebo: 18.3 [95% confidence interval (CI), 10.9-not evaluable] versus 5.4 (95% CI, 3.7-5.7) months [hazard ratio (HR) = 0.32; 95% CI, 0.23-0.45; P < 0.0001], and a similar PFS benefit was observed in patients receiving an ISD, regardless of BRCA mutation status. Grade ≥3 treatment-emergent adverse events occurred in 50.8% and 19.3% of patients who received niraparib and placebo, respectively; the most common events were neutrophil count decreased (20.3% versus 8.0%) and anemia (14.7% versus 2.3%).

**Conclusions:** Niraparib maintenance treatment reduced the risk of disease progression or death by 68% and prolonged PFS compared to placebo in patients with platinum-sensitive recurrent ovarian cancer. Individualized niraparib dosing is effective and safe and should be considered standard practice in this setting.

# Calendar of Virtual Monthly Clinical Meetings 2021-22

| | |
|---|---|
| 28th May, 2021 | B L Kapoor Hospital |
| 25th June, 2021 | All India Institute of Medical Sciences |
| 30th July, 2021 | Sitaram Bhartia Hospital |
| 3rd September, 2021 | Army Hospital (Research & Referral) |
| 24th September, 2021 | Deen Dayal Upadhyay Hospital |
| 29th October, 2021 | PGIMSR & ESI Hospital |
| 19th - 21st November, 2021 | 43rd Annual Conference |
| 26th November, 2021 | MAMC & Lok Nayak Jai Prakash Narayan Hospital |
| 31st December, 2021 | Sir Ganga Ram Hospital |
| 28th January, 2022 | ABVIMS & Dr Ram Manohar Lohia Hospital |
| 25th February, 2022 | UCMS & Guru Tek Bahadur Hospital |
| 25th March, 2022 | VMMC & Safdarjung Hospital |
| 29th April, 2022 | LHMC & Smt. Sucheta Kriplani Hospital |
| 27th May, 2022 | Apollo Hospital |

# Proceedings of Virtual AOGD Monthly Clinical Meeting held at Deen Dayal Upadhyay Hospital on 24th September 2021

## Clinical Profile of COVID-19 Obstetric Patients Admitted to a Tertiary Care Hospital during the Two Waves

**Ritu Goyal, Pinkee Saxena, Rikita Jindal Monika Suri Grover**

COVID-19 has become a major global health threat. Since its first identification in Wuhan China in December 2019, it has spread globally at an accelerated rate with rapid increase in cases and mortality. India has witnessed two waves of this pandemic. The first wave was from July- December 2020 and second was from March-May 2021. We studied the clinical profile of the obstetric patients admitted during the two waves of COVID 19 in our hospital. Retrospective data was collected and statistical analysis was done.

There were 45 COVID-19 obstetric patients in wave one and 46 COVID-19 obstetric patients in wave two. There was no difference in the age or parity in the two groups. Patients mainly presented in the third trimester. Most patients in wave 1 were asymptomatic where as a significant number of patients in the second were symptomatic. Most common symptoms were cough and fever. In the first wave none required ICU admission whereas in the second wave 11 patients required ICU admission. Course of pregnancy and fetal outcome were similar in the two groups. There were 10 maternal deaths in the second wave of covid.

**Conclusion:** The second wave of COVID 19 was more virulent, required more oxygen and ICU admissions and was associated with increased mortality.

## A Rare Case of Pyoperitoneum in Term Pregnancy

**Harvinder Kaur, Soma Mitra, Pinkee Saxena, Sunita Seth, Rita Ranjan**

**Case:** A 24 year old primigarvida with 39week of gestation was admitted with pain abdomen which was non radiating, dull in nature. Patient had similar episode of pain abdomen off and on in past one month. There was no other significant positive history. It was spontaneous conception after 3years of marriage. On examination, she was of average built with a normal BMI. Her general and systemic examinations were normal. Tenderness and fullness was observed in the epigastric region. Obstetrics examination revealed a single live fetus in cephalic presentation. All her investigations were normal at time admission including ultrasound. He progress of labour was slow and she underwent LSCS for Non Progress of labour. On opening of abdomen copious pus was observed in the abdominal cavity which was non billous and non faecal. Baby was delivered. Liquor was clear, tubes and ovaries were normal. Exploration of abdomen showed no perforation either of small or large bowel and all solid organs were intact. Omental thickening was noted. Omental and lymph node biopsy were taken. Patient had continuous fever in the post-operative period. All her investigations were normal and all culture sterile. AFB and CBNAAT were negative. Patient was empirically started on ATT, to which she responded in seven days. Meanwhile her HPE report showed necrotising granuloma which was positive for AFB.

TB is an ancient disease. But still there are challenges in its diagnosis especially in pregnancy due to the nonspecific nature of symptom and delay in utilising investigative modalities. Diagnosis of abdominal TB is further challenging because of paucibacillary nature. Hence a high index of suspicion should be kept in mind. Active TB has adverse maternal and fetal outcome. Management of TB in pregnancy is similar as in nonpregnat state with respect to composition and dosage of the antitubercular drugs. In cases of pyoperitoneum, if no obvious cause found, tissue biopsy should be taken to increase the chance of diagnosis. Offering early diagnosis and prompt treatment ensures better maternal and perinatal outcome.

## Role of Prostate-Specific Antigen in PCOS

**Shashi Lata Kabra, Pankti R Ghelani Soma Mitra, Pinkee Saxena**

Prostate-specific antigen is a glycoprotein expressed by both normal and neoplastic prostate tissue. It is

produced under the regulation of the stimulatory effects of androgens, progestins, glucocorticoids, and inhibitory effects of estrogens. PSA is used as highly specific and valuable marker for screening, diagnosis and monitoring of prostatic adenocarcinoma. Recent development of ultrasensitive assays demonstrated PSA in a wide variety of female tissues and fluids such as the ovary, breast, amniotic fluid and milk. PSA expression in females is stimulated by androgens and progestin. PSA levels increase in women with androgen excess. Elevated serum PSA in females with hyperandrogenism including those with PCOS, has become a subject of clinical interest with PSA being suggested as a marker of hyperandrogenic state. The present study was taken up to evaluate serum PSA levels in patients with PCOS.

**Objective:** The Study was undertaken to evaluate the level of serum total PSA levels in patients of PCOS.

**Material and Method:** The case-control study included 40 women with PCOS diagnosed on the basis of revised Rotterdam 2003 criteria and 40 age matched healthy women as controls. Serums PSA were measured along with Follicle Stimulating Hormone, luteinizing hormone, DHEAS, Testosterone, Prolactin, Thyroid stimulating hormone and Ultrasound pelvis.

**Result:** The total serum PSA levels were not found to be significantly elevated in study group (0.014±0.007ng/mL) as compared to the control group (0.012±0.007 ng/mL, p-value 0.08). Total serum PSA level had an inverse correlation with serum FSH levels with r value -0.41 and p value between two groups <0.01. Total testosterone levels were found to be 0.91±0.31ng/ml and 0.70±0.30 ng/ml, DHEAS values were found to be 362.36±137.64 µg/ml and 136.66±55.73 µg/ml in PCOS and controls, respectively.

**Conclusion:** The present study which was done in Indian population concludes that there is no difference in the serum levels of PSA with and without PCOS. Further Indian studies are required to arrive at any conclusions.

# Quiz Held at Monthly Clinical Meeting

**Rekha Bharti[1], Niharika Guleria[2]**
[1]Senior Resident, [2]Professor, VMMC & Safdarjung Hospital

1. **Stress leading to bladder pressure more than urethral pressure can cause incontinence due to**
   a. Intrinsic sphincteric deficiency (ISD)
   b. Neurogenic detrusor activity
   c. Nonneurogenic detrusor activity
   d. None of the above
2. **Defecatory dysfunction i.e constipation and incomplete emptying affects**
   a. 20% of women in general population
   b. 5% of women in general population
   c. 30-40% of women with POP
   d. None of the above
3. **According to current recommendations mesh and tape implants are**
   a. To be immediately withdrawn from market
   b. Not indicated in high risk women
   c. Safe option in majority of women
   d. All of the above
4. **A 5-10% reduction in baseline weight results in approximately**
   a. 20% reduction in frequency of incontinence
   b. 30% reduction in frequency of incontinence
   c. 40% reduction in frequency of incontinence
   d. 50% reduction in frequency of incontinence
5. **Recurrent UTI is 2 uncomplicated UTIs in six months or 3 positive cultures in preceding 12 months.**
   a. True
   b. False

**Answers**

| | | |
|---|---|---|
| Q. 1- a | Q. 2- a | Q. 3- c |
| Q. 4- d | Q. 5- a | |

## Winners of the Monthly Clinical Meeting Quiz October Issue 2021

**Dr Pratibha Singh Rajput**
Secondary DNB Resident, Deen Dayal Upadhyay Hospital

**Dr Sukanya Sanapala**
Resident, Obstetrics & Gynaecology, VMMC & Safdarjung Hospital

**Dr Akhila Shankar**
Resident, Obstetrics & Gynaecology, Deen Dayal Upadhyay Hospital

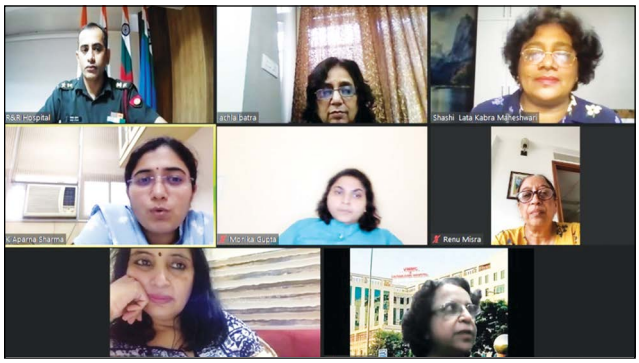
# Events Held in September 2021

| S.No. | Date | Event | Time |
|---|---|---|---|
| 1 | 03.9.2021 | AOGD Clinical Meeting at Army Hospital, Research & Referral | 4:00 pm - 5:00 pm |
| 2 | 04.9.2021 | Public Forum on White Discharge in Women by WOW India, AOGD & DGF | 4:00 pm - 5:00 pm |
| 3 | 05.9.2021 | Public Forum: Adolescent Health Awareness, by Outreach Team AOGD with RUFAIDA Nursing College | 3:00 pm - 4:00 pm |
| 4 | 08.9.2021 | "Bursting the Myths and realities of RPL" by FOGSI Food & Drug & Medico Surgical Equipment committee with Infertility Subcommittee AOGD | 5:00 pm - 7:30 pm |
| 5 | 10.9.2021 | "Fetal Anomalies Workshop- Meeting the Expectation" by Fetal Medicine and Genetics Subcommittee | 3:00 pm - 6:00pm |
| 6 | 14.9.2021 | "Contraception: Still Challenges & Barriers" by SMLM under aegis of AOGD | 6:00 pm - 8:00pm |
| 7 | 15.9.2021 | **"**The Truth about Thyroid" by Viveo under aegis of Infertility Subcommittee AOGD | 5:30 pm - 7:00 pm |
| 8 | 16.9.2021 | "Making Child Birth a Positive Experience" by Safe Motherhood Subcommittee AOGD | 4:30 pm - 7:00 pm |
| 9 | 17.9.2021 | "Decoding the Basics of Prenatal Screening" by QI Subcommittee AOGD & PAN DGF | 3:00 pm - 5:00 pm |
| 10 | 18.9.2021 | Switch Symposia on 'Prevention & Management Update for Postpartum Haemorrhage" by AOGD | 2:00 pm - 4:00 pm |
| 11 | 20.9.2021 | "Critical Period after Delivery" by Multidisciplinary Subcommittee AOGD, in association with DGFSW & ESI PGIMSR, Basai Darapur | 4:00 pm - 6:00 pm |
| 12 | 21.9.2021 | CME on Contraception by SGRH | 6:00 pm - 8:00 pm |
| 13 | 21.9.2021 | "Menopause- Pause to life?" by AIIMS, Delhi, FOGSI Urogynae committee & AOGD | |
| 14 | 23.9.2021 | "Simple solutions to Avoid Complex Problems in Laparoscopy Gynecology" by Endoscopy Subcommittee AOGD | 6:00 pm - 8:00 pm |
| 15 | 24.9.2021 | AOGD monthly clinical meeting at DDU Hospital | 4:00 pm - 5:00pm |
| 16 | 25.9.2021 | "Endometrial Cancer Surgical Treatment and Beyond" by UCMS & GTB Hospital under aegis of Oncology Subcommittee | 3:00 pm - 5:00pm |
| 17 | 27.9.2021 | Adolescent Health & Nutrition counseling to celebrate Poshan Maah by Rural Health Subcommittee | 11:00 am - 1:00 pm & 3:00 pm - 5:00 pm |
| 18 | 28.9.2021 | "Heart Disease in Pregnancy: by AOGD & FOGSI Medical Disorder Committee | 5:00 pm - 7:00 pm |
| 19 | 29.9.2021 | "Adolescence- A time of Opportunities & Woes" by AOGD Adolescent Health Subcommittee | 5:00 pm - 7:00 pm |
| 20 | 30.9.2021 | "Male Sexual Disorders" by FOGSI Sexual Medicine Committee under aegis of Infertility Subcommittee AOGD | 6:00 pm - 8:00 pm |

# Forthcoming Events for October 2021

| S.No. | Date | Event | Time |
|---|---|---|---|
| 1 | 01.10.2021 | Module-1 "Hyperglycemia in pregnancy: Preconceptional care and Screening by Safe Motherhood Subcommittee | 5:00 pm - 7:00 pm |
| 2 | 02.10.2021 | "Conservative management of Pelvic Organ Prolapse & Urinary Incontinence" by Urogynae Subcommittee | 11:00 am - 1:00 pm |
| 3 | 05.10.2021 | "PPH Preparedness– Road to Maternal safety" by AOGD | 5:00 pm - 7:00 pm |
| 4 | 08.10.2021 | "Endometriosis and Infertility" by Endometriosis Subcommittee | 3:00 pm - 5:00 pm |
| 5 | 09.10.2021 | Webinar on Theme: "PGT India- A Dream Come True" by Fetal Medicine & Genetics Subcommittee | 7:00 pm - 9:00 pm |
| 6 | 16.10.2021 | "Luteal phase defect" by AOGD (Physical Meet) | 3:00 pm - 5:00 pm |
| 7 | 21.10.2021 | "Fertility preservation theme" by Adolescent Subcommittee with DGF-SW | 5:00 pm - 7:00 pm |
| 8 | 21.10.2021 | Public form by Outreach Subcommittee | 4:00 pm - 5:30 pm |
| 9 | 28.10.2021 | "Tubal Corrective Surgeries; The Use Of Endoscopy" by Endoscopy Subcommittee | 6:00 pm - 8:00 pm |
| 10 | 29.10.2021 | AOGD monthly clinical Meeting at ESI Hospital | 4:00 pm - 5:00 pm |
| 11 | 30.10.2021 | "Management of Cervical Cancer: Nuances and Changing Perspectives" by Oncology Subcommittee | 5:00 pm - 7:00 pm |

# Events held under the aegis of AOGD in September 2021



Monthly Clinical Meeting- Army Hospital

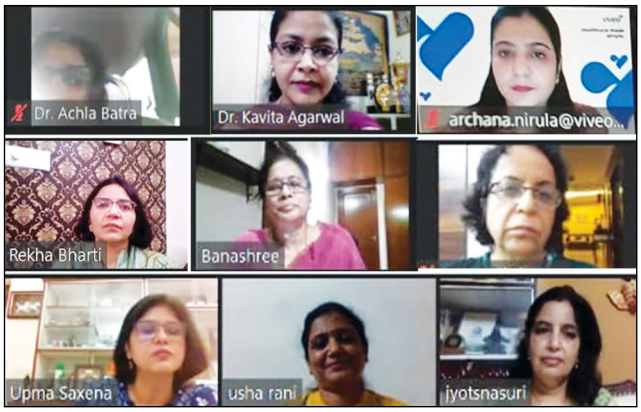
Public Forum on Vaginal Discharge in Women


Adolescent Health Awareness


"Bursting the Myths and realities in RPL"

"Fetal Anomalies Workshop- Meeting the Expectation"

"Contraception- Challenges & Barriers"




"The Truth About Thyroid"


"Making Childbirth a Positive Experience"

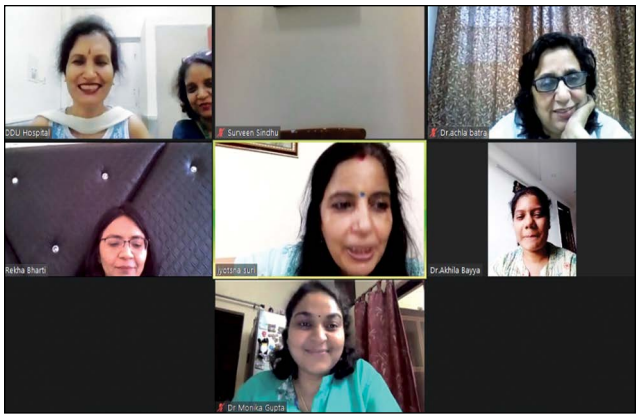
"Decoding the Basics of Prenatal Screening"

"PPH- Prevention & Management"

"Critical Period after Delivery"


"Menopause- Pause to Life?"


Safe Laparoscopic Surgery

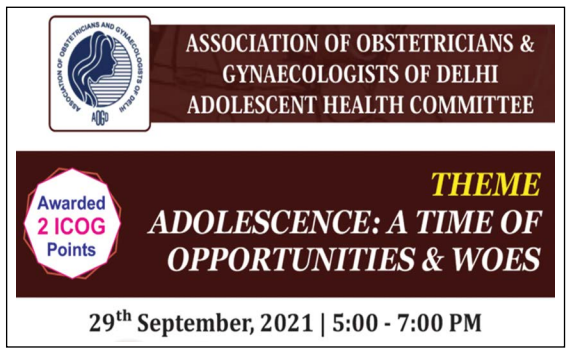



Monthly Clinical Meeting DDU Hospital

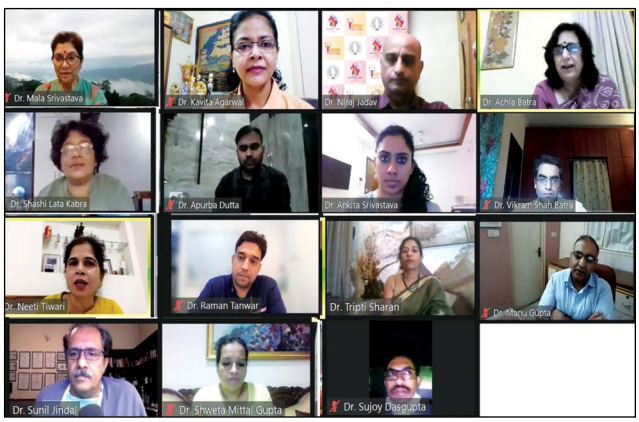

"Endometrial Cancer- Surgical Treatment & Beyond"


"Adolescent Health & Nutrition Counseling"


"Heart Disease in Pregnancy"




"Adolescence - A time of Opportunities & Woes"




"Male Sexual Disorders"


"MTP Acts: New Amendment Implementation"

# Association of Obstetricians & Gynaecologists of Delhi

## MEMBERSHIP FORM

Name:.....

Surname: .....

Qualification (Year): .....

Postal Address: .....

City:..... State: ..... Pin code: .....

Place of Working:.....

Residence Ph. No. ..... Clinical / Hospital Ph. No.....

Mobile No:.....Email: .....

Gender: Male:.....Female:.....

Date of Birth: Date..... Month ..... Year .....

Member of Any Society:.....

Proposed by: .....

Cheque/DD / No: .....

Cheque/Demand Draft should be drawn in favour of: **Association of Obstetricians & Gynaecologists of Delhi**

**For Online Transfer Through NEFT/RTGS**
Name of Bank: **Central Bank of India**
Branch: **Lady Hardinge Medical College Branch**
Name of Account: **Association of Obstetricians and Gynaecologists of Delhi**
Account No: **3674596638**
IFSC Code: **CBIN0283462**
MICR Code: **110016067**

For Life Membership : Rs. 11,000 + Rs. 1,980 (18% GST applicable) = Rs. 12,980
For New Annual Membership* : Rs. 2,000 + Rs. 360 (18% GST applicable) = Rs. 2,360
For Old Renewal Membership+ : Rs. 1,200 + Rs. 216 (18% GST applicable) = Rs. 1,416

**Encl.: Attach Two Photocopies of All Degrees, DMC Certificate and Two Photographs (Self attested)**
***-Annual Membership is for the calendar year January to December.**
**+ - In case of renewal, mention old membership number.**
**Note: 18% GST will be applicable as FOGSI requires it.**

Send Complete Membership Form Along With Cheque / DD and Photocopy of required documents.


## AOGD SECRETARIAT

Room Number 001, Ward 6, Department of Obstetrics & Gynaecology
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