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Review Article

Diagnostic and Management Challenges of Endometrial Tumours in Developing Countries!

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Abstract:

Gynaecological cancers are among the most common cancers in women and hence an important public health issue in very country. Ovarian, Cervical, and Endometrial cancers contribute the most of Gynaecological cancers in India and worldwide. Endometrial benign tumours like Endometrioid cystadenoma / adenofibroma with endometrioid type glands, associated with endometriosis pose challenges of diagnosis.

Endometrial cancer (EC) is the most common gynaecological malignancy in the West, but in India, the incidence rates are low. National cancer registry project (NCRP) estimated 27,922 cases of EC in 2022 in India. The possible association between cancer and endometriosis varies according to the histologic subtype of ovarian cancer and is focused mostly on endometroid and clear-cell ovarian cancer subtypes.

The only way to diagnose womb cancer for sure is to take a sample of the tissue lining the womb (biopsy) and get histopathology report. However, most of the literate and urban women with ECs present at an early stage due to menorrhagia, abdominal pain or abdominal distension and are associated with a good prognosis. But the situation in rural India is one of lack of diagnostic and management facilities in public sector even at most of the district level. Treatment for endometrial cancer usually involves a hysterectomy, and adjuvant radiotherapy and/or chemotherapy. Surgery sometimes may include the removal of uterus and the fallopian tubes and ovaries, called a Hysterectomy with salpingo-oophorectomy. Adjuvant Radio/Chemotherapy treatment is planned based on final surgical &pathological staging.

Due to the lack of cancer awareness, variable pathology, and dearth of proper screening facilities in most developing countries including India, most rural women report at advanced stages, adversely affecting the prognosis and clinical outcomes.

Materials and Methods: This article is based on a case of adenocarcinoma Stage 1, Type 2 and another case of Endometrioid Cyst clinically and radiologically suspected to be malignant, but histopathology of tissues tested branded it as Endometrioid Cyst Adenofibroma. Relevant literature review of global experiences and good practices of management of endometrial cancers are added.

Keywords: gynaecological malignancies; cross-disease analysis; endometrial cancer; endometriosis; genome-wide association study; genetic correlation; role of obesity; party

Introduction

About five lakh women develop Gynaecological Cancers worldwide every year and more than one lakh new patients are diagnosed in India itself. Gynaecological cancer is defined as uncontrolled growth and spread of abnormal cells that originate from the reproductive organs like uterus, fallopian tubes, and ovaries. Gynaecological cancers are among the most common cancers in women and hence an important public health issue. Due to the lack of cancer awareness, variable pathology, and dearth of proper screening facilities in most developing countries including India, most women (except for urban literate women) report at advanced stages, adversely affecting the prognosis and clinical outcomes. Ovarian, Cervical, and Endometrial cancers contribute the most of Gynaecological cancers in India and worldwide [1,2,3,4,5]. Ovarian cancer (OC) has emerged as one of the most common malignancies affecting women in worldwide and India and has shown an increase in the incidence rates over the years. Ovary cancer (OC) is one of the most common lethal and aggressive gynaecologic cancers. It still is amongst the commoner cancers in India and a leading cause of cancer-related deaths in women [12]. The traditional treatment of OC involves resecting all suspected organs followed by chemotherapy. Cervical cancer (CC) is the second most common cancers of women in India, despite

being largely preventable and national Cervical cancer (CC) detection campaigns promoted by GOI. However, cervical cancer is on a declining trend, though it remains the second most common cancer in women after breast cancer [12]. Among 604,100 new cases of CC and 341,831 deaths due to this malignancy detected globally in 2020, India, accounted for 9.4% of all cancers and 18.3% (123,907) of new cases in 2020. The age-standardized incidence rate of cervical cancer decreased substantially by about 40% between 1990 to 2016, but it is still the second leading cause of cancer deaths for females in 12 Indian states [2]. Every year in India, about 150,000 women are diagnosed with cervical cancer and half of the die from this disease. Endometrial cancer (EC) is the most common gynaecological malignancy in the West, but in India, the incidence rates are low. Most of these ECs in urban India present at an early stage and are associated with a good prognosis. The symptoms of Menorrhagia, postmenopausal spotting or vaginal bleeding, abdominal pain and distension alert the literate urban women who seek consultations with obstetrics and Gynaecologist's. however, in Rural India lack awareness, and lack of diagnostic and management facilities in public sector delay detection and treatment. The association between endometriosis and cancer is focused mostly on ovarian cancer, - endometroid and clear-cell ovarian cancer subtypes. The possible association between cancer and endometriosis varies according to the histologic subtype of ovarian cancer [6,7].

Ovarian and endometrial cancer have a strong genetic correlation [9]. Knowing about inheritance of a cancer-related gene helps to determine a plan for early detection and prevention. The risk of endometrial cancer is more in women above 50 years of age, women with diabetes, high blood pressure, and overweight. The high levels of oestrogen hormone in obese women lead to endometrial cancer [13,14,15,16]. Other risk factors include menstruating before 12 years of age, irregular ovulation, and use of tamoxifen for treating breast cancer. Unusual bleeding from the vagina after menopause is the most common sign of endometrial cancer. Endometrial cancer incidence is reported to be around 5 per 1000 women from hospital-based studies [5]. One thirds of the cases are among nulliparous and 1-2 gravida women. Increasing age is the first and most important risk factor followed by Hormone therapy, Postmenopausal Oestrogenic therapy, Selective oestrogen receptor modifiers, Tamoxifen therapy, Obesity, Metabolic syndrome, Diabetes, Nulliparity, Early menarche or late menopause, Polycystic ovary syndrome, Family history/genetic predisposition, Mother, sister, or daughter with uterine cancer, Lynch syndrome and Endometrial hyperplasia. Indian experience so far reports that endometrial cancer patients with localized disease at diagnosis have a good outcome, even cure is possible if it is detected in early stages and treated with surgery either alone or with hormones of oestrogen and progestin combination is given to the patient. Progestin helps in protecting the lining of uterus from oestrogen while the growth of the endometrium is stimulated by oestrogen. If progestin is not given in hormone replacement therapy for endometriosis there is increased risk of endometrial carcinoma [9].

The most common types of treatment for women with endometrial /uterine cancer include: i) Surgery- Total Hysterectomy (Uterus, Salpingo-Oopherectomy) ii) Radiation Therapy iii) Chemotherapy iv) Hormone Therapy, v) Targeted Therapy and vi) Immunotherapy for Endometrial Cancer [1,7,8].

The surgical treatment comprises of removal of uterus, sometimes, ovaries and Fallopian tubes also. Select cases are given adjuvant radiotherapy and/or chemotherapy depending on the final surgical-pathological staging of the biopsies of the removed organ's histopathological testing.

Case Reports:

1.A case of Uterine endometrial Adenocarcinoma:

Roopa aged 56 years, sought a gynaecologist's consultation for heavy Bleeding per vagina for 6 months, who referred her to a private Oncology Hospital in Mysuru, Karnataka on 18 October 2023. She has a married life of 30 years and has a daughter aged about 26 years. She attained menopause since 2012. Her general condition was fair, but BMI was 32. An USG abdomen with transvaginal Scan done on 16/10 23 showed Bulky Uterus with thickened endogenic endometrium with cystic spaces suggestive of endometrial hyperplasia. CT Scan done of the abdomen prior to coming to this hospital reported to be normal. Her basic investigations included: Hb%=12g/Dl, Urea = 30 mg/Dl, Creatinine= 4.4 mg/dl, Sodium =140 mEq /l, Potassium=4.4 mEq/dl, Chlorine=120 mEq/dl, Total WBC count 10.400/Cu mm, Neutrophils= 86%, Lymphocytes = 12%, Eosinophils=2% and Platelet count+2.41,000/cu mm. 2 D echo reported heart, functions as normal with mild Mitral Regurgitation with 60% EF.

Endometrial biopsy: Indicated moderately differentiated adenocarcinoma Stage 1, Type 2.

Surgery Done: A exploratory Laparotomy was done under GA. The uterus was normal, bilateral fallopian tubes and ovaries were in internal iliac fossae and appeared normal. Bilateral lymph nodes were seen. A total Hysterectomy, Bilateral salpingo-oophorectomy was done and after a thorough pelvic peritoneum search, bilateral Pelvic lymph nodes (Right side=4, Left side=2) were dissected and removed. Specimens of uterus (8.5x4x3.5 cms), Right ovary (2x1x1 cms) and Left ovary (2x1x1cms) and both sides ovarian tubes and lymph nodes were sent for Histopathology. Post-operative recovery was uneventful. A clinical review on 3/11/2023 was normal. Histopathology report received on 6 November confirmed that the main tumour was in endometrium of a size of 1x 0.5cm. The tumour type was described as Endometroid adenocarcinoma, well differentiated Grade I, and it had infiltrated less than half of Myometrium thickness. Lymph vascular invasion (LVI - refers to the involvement of small lymphatic or blood typically venous vessels by tumours cells) and Perineural invasion (PNI- growth of tumours in, around, and through nerves and nerve sheaths) were absent. Cervical stroma was uninvolved, and myometrium and Serosa were free of tumour. Both ovarian tubes were unremarkable. Thus, histopathology confirmed endometrioid adenocarcinoma, with no secondaries in any other specimens examined.

As of 15 November 2023, Roopa is doing fine and has been advised quarterly follow-ups.

2. Radiological Ovarian Cancerous Cyst, turned Endometrioid Cyst-adenofibroma

1. Current Illness & History: Pragati a 45-year-old lady complained of abdominal distension for the last 3 months and started having post-menopausal bleed since March 2023, 4 years after the menopause. She sought the opinion of a gynaecologist on 12th September 2023, as she started getting exhausted during her routine Badminton games for 3 months along with abdominal distension. Gynaecologist's report read- the lady short, a bit overweight, but pleasing personality. The abdominal bloating was visible more to the left side. Basic investigations done were- Complete Blood count (CBC), Pap smear and CT scan of abdomen and Pelvis were done. Results were: 1. CBC indicated Leucocytosis 11.65cell/microliter (normal=4-10), Lymphocytes 44% (N=40%), Hb%=12.4 g/Dl (N=12-5). CA-125-68, CEA-2.4 CA 19-9:240, Serum Albumin 4.2mg/Dl, Glbulin-2.7 g/Dl Alb; Glob Ratio=1.6. Provisional diagnosis was recurrent endometritis ovarian cyst most probably malignancy. An exploratory Laparotomy was recommended in a facility with Frozen section histopathology, to go for extended surgical dissection if needed.

Previous History: Married life for 22 years and a daughter of 20 years old. She had undergone Right partial Ovariotomy and Salpingectomy and Left salpingo-oophorectomy for endometriosis in 2012.

2. PAP smear: Cervix bled minimal on touch. Microscopy saw - Plenty of Coccobacilli and clue cells were seen. No epithelial cell abnormalities were reported.

3. USG & CT scan -Abdomen and Pelvis 914/09/23): USG revealed large left adnexal cyst more in favour of Ovarian malignancy. Transvaginal CT scan of abdomen and Pelvis revealed large (127 X 154 X 191 mm sized)

ovarian neoplasm. A complex predominantly cystic lesion with multiple thick enhancing internal septations in the pelvis and lower abdomen. No Ovaries were seen. Uterus size was normal. All other abdominal organs were normal. Posterior -displacement and compression of the left lower ureter by the pelvic lesion, causing mild left obstructive hydroureteronephrosis, with no significant enlargement lymph nodes or ascites.

Surgery:

The family had to change 2 hospitals in search of a facility, with a surgical team of an Obstetrician, a General cum Laparoscopic surgeon, an Onco-surgeon, and an anaesthetist to handle expected extensive adhesion and back-end team of Physician, radiologist and histopathologist with frozen section examination facility. Surgery done in Apollo Hospital, Bengaluru, first anterior abdominal wall opened in layers, a large solid cyst noted with dense extensive adhesions completely distorting the anatomy. Gradual dissection done and ovarian mass in left adnexa (18x13x12 cm) was removed and sent for frozen section. The cyst had to be drained partially of thick brownish haemorrhagic fluid. Then the posterior rectal adhesions to uterus were released and ovary were dissected with great difficulty separating the adhesions by both surgeons and the gynaecologist and were also sent for histopathology. The summary of surgery reads Exploratory Laparotomy +Extensive adhesiolysis + Left Ovary Cyst removal +Frozen section + Total abdominal Hysterectomy under spinal Anaesthesia.

The histopathology report:

1. Frozen section: Benign endometrial cyst- received in an hours' time to limit surgical intervention to releasing adhesions and removal of utters and the Cyst,

2. The Uterus and Cervix revealed i) Endocervical lining sowing papillary hyperplasia with focal squamous metaplasia. There was no evidence of dysplasia or Malignancy in sections studied. Final Diagnosis: Endometrioid Cyst Adenofibroma

Post-operative recovery was uneventful. The abdominal sutures were removed in stages on 10th and 16th after surgery and no post-operative complications. Pragati has fully recovered after 4 weeks. As of 15 November 2023, she is doing fine.

Discussions:

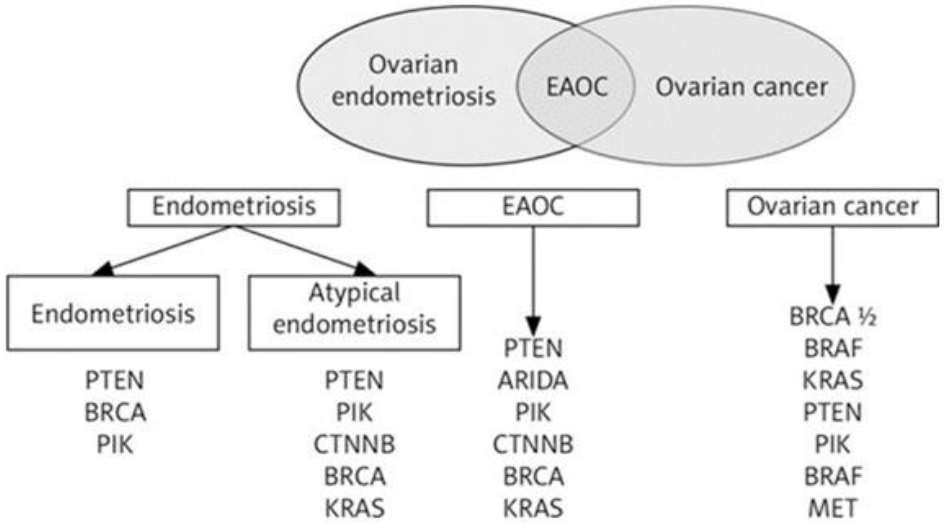
Gynaecological cancers are among the most common cancers in women, difficult to diagnose and treat for want of diagnostic facilities in most developing countries. The drudgery of women due to this disease is more due to social stigma as most poor and illiterate women consider the symptoms as normal of aging and delay seeking care despite being almost curable in early stages. Therefore, it is of an utmost public health important issue in very country. Endometrial cancer is common in western women, and the rates are very high probably due to care seeking behaviour and diagnostic facilities. However, in India, the rates are as low as 4.3 per 100,000 adult and elderly women.

Increasing age is the first and most important risk factor as for most cancers. Other risk factors for endometrial cancer include Hormone therapy, Postmenopausal Oestrogenic therapy, Selective oestrogen receptor modifiers, Tamoxifen therapy, Obesity, Metabolic syndrome, Diabetes, Nulliparity, Early menarche or late menopause, Polycystic ovary syndrome, Family history/genetic predisposition, Mother, sister, or daughter with uterine cancer, Lynch syndrome and Endometrial hyperplasia [3].

There are hardly any community-based studies to define incidence or prevalence. A hospital-based study from Mumbai, reported that the endometrial cancer patients with localized disease at diagnosis had a good outcome in India, as the proportions of patients dying above 50 years of age, non-residents and illiterates was higher than their counterparts. Only about half (54.8%) of patients had some form of treatment before attending the hospital. The contribution of tobacco-chewers (4.2%) and family history of cancer (6.1%) was small. Whereas, among the patients a quarter (25.8%) had 3-5 pregnancies (gravida), Nulliparous to Gravidae 1 or 2 were 36.1%, and 38.1% did not even remember the pregnancy history correctly. The 5-year overall survival rate was 92%, which also indicated better prognosis for those aged less than 50 years (97%), with localized disease (93%) and those treated with surgery either alone or as a combination with hormones (95%). [5].

Endometriosis Associated Cancers and Genes Involved:

A review of the literature suggested a link between endometriosis and ovarian and Uterine cancers, but not breast and cervical cancer. Women with endometriosis appear to be more



likely to develop, non-Hodgkin's lymphoma, and brain tumours cancers. Some case reports, indicate the complexity of the endometriosis-cancer relationship. A case of primary endometrioid carcinoma arising from deep infiltrating endometriosis 6 years after diagnosis of ovarian cancer is reported. Somatic mutations of PIK3CA, PTEN, and ARID1A might play a role in the disease progression and malignant transformation. At present, not

a single marker is recommended for diagnosis, or treatment. The issue of how to identify which endometriosis patients develop ovarian cancer remains critical but unanswered [10,11].

The likelihood of developing endometrial polyps and uterine fibroids is higher among postmenopausal women with proliferative endometrium, according to a study published in the December 2023 issue of the journal Maturitas [20].

A cross-sectional study of all women with a tissue-proven diagnosis of endometriosis postoperatively in a tertiary care hospital over a decade between January 1, 2010, and December 31, 2019, reported that out of 800 patients, 104 (13.0%) were found to have coexistent malignancy. Among 104 total cancer cases i) ovarian cancer contributed 50, (6.2%); ii) endometrial cancers 33, (4.1%); iii) synchronous ovarian, endometrial 7, (0.9%); and breast cnacers-14, (1.8%). Postmenopausal status (Odds Ratio-OR= 6.2), duration of endometriosis over 5 years (OR 4.7), and endometriomas larger than 8 cm, increasing age over 50 years (OR 1.13), higher levels of cancer antigen 125 (CA 125 -OR 1.002), were inferred as predictive of coexistent malignancy [6].

A study of a total of 1808 postmenopausal women who underwent endometrial biopsy between January 1997 and December 2008 and followed-up for a comparable duration of 11.9 vs. 11.5 years, respectively., indicated that Endometrial polyps developed twice more often in women with proliferative endometrium (17.3%) as compared to women 9.7% in women with atrophic endometrium (9.7%). On multivariable analysis, 62.1% of women with

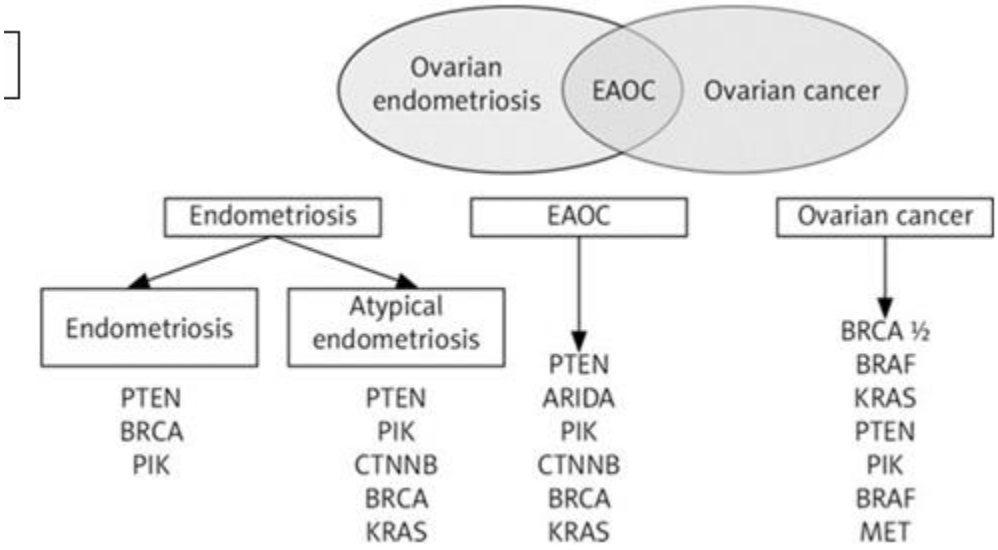


Figure:1 proliferative

endometrium were found to have fibroids on ultrasound compared to 50.3% of women with atrophic endometrium. The risk of endometrial polyps was 2-folds higher among women with proliferative endometrium with adjusted odds ratio (OR) of 1.9. The need for repeat endometrial biopsy was 34.9% in women with proliferative endometrium vs 16.8% in those with atrophic endometrium. Nearly a quarter (26.6%) of women in the proliferative endometrium group required hysterectomy or hysteroscopy as against 16.2% in the atrophic endometrium group. The study inferred that women with proliferative endometrium are at higher risk of malignancy, endometrial polyps, and uterine fibroids. Therefore, the authors recommend medical management to reduce estrogenic activity and associated risks in postmenopausal women with proliferative endometrium [10,11].

Pathological types: Endometrioid cystadenoma / adenofibroma are benign tumours with endometrioid type glands, associated with endometriosis, which is represented by our Pratim's case, that needs to be differentiated with endometrial cancers only by a pathophysiologic perspective. Endometrial carcinomas have been traditionally divided into 2 types: Type 1: includes endometrioid and mucinous carcinoma and Type 2: includes serous, clear cell, undifferentiated carcinoma and carcinosarcoma. Endometrioid histotype constitutes approximately 80% of all endometrial carcinomas, most of which are low grade (FIGO grade 1 - 2), as was our Case of Roopa was one such report [13]. Surgical treatment for both conditions remains basically the same.

Type 1: These lesions are associated with long term elevated oestrogen levels, which lead to persistent proliferative stimulation of the endometrium. Risk factors leading to hypoestrogenism include obesity, exogenous hormonal therapy (e.g., tamoxifen use for breast cancer), ovarian cortical hyperplasia / hyperthecosis, polycystic ovarian syndrome and hormone producing tumours (e.g., granulosa cell tumour of the ovary). Among others PTEN, ARID1A, PIK3CA, KRAS gene alterations are common. Atypical endometrial hyperplasia / endometrioid intraepithelial neoplasia is regarded as the precursor lesion [2,3,4].

Type 2: These tumours have a lesser association with unopposed oestrogen exposure. Serous carcinoma is characterized by early alterations in TP53. Precursor lesion for clear cell carcinoma has not been identified yet but are faster growing and more likely to spread [10].

Sites involved: Most common site is the uterine corpus - endometrium, endometrial polyps or adenomyosis. Primary cervical endometrioid adenocarcinomas are extraordinarily rare and likely develop from cervical endometriosis. Drop metastasis or contiguous extension from corpus should be ruled out in these cases. Technically, any tissue involved.

All endometrial cancers must perform a complete molecular classification (POLE mut, MMRd, NSMP, p53abn) says the FIGO report of June 2023.

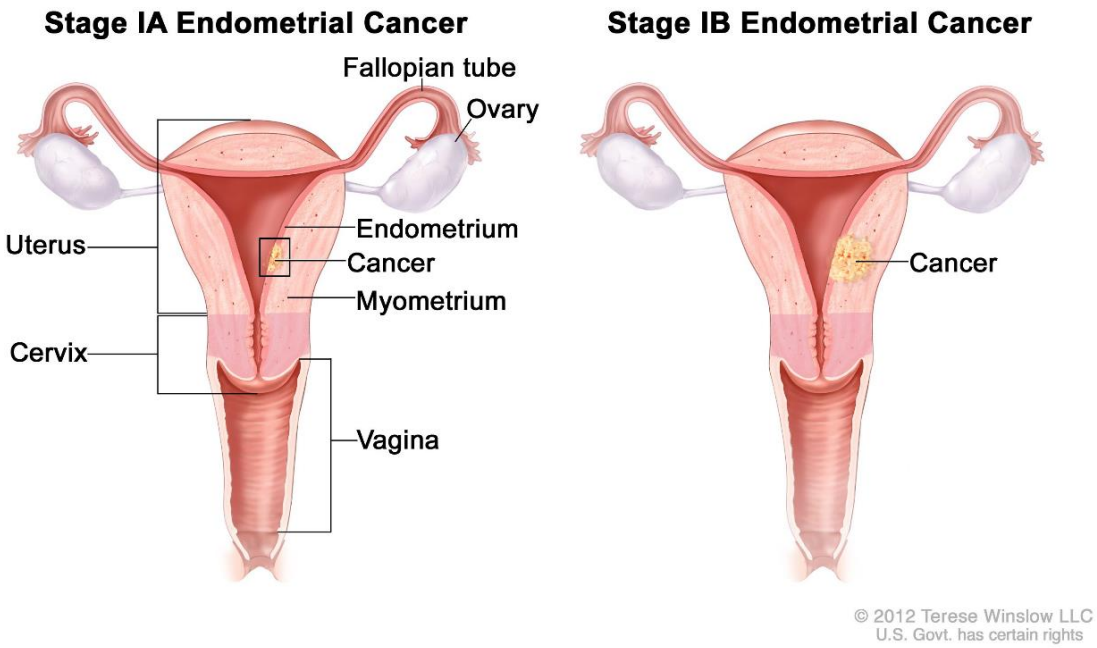


Figure 2: FIGO classification Illustrated:

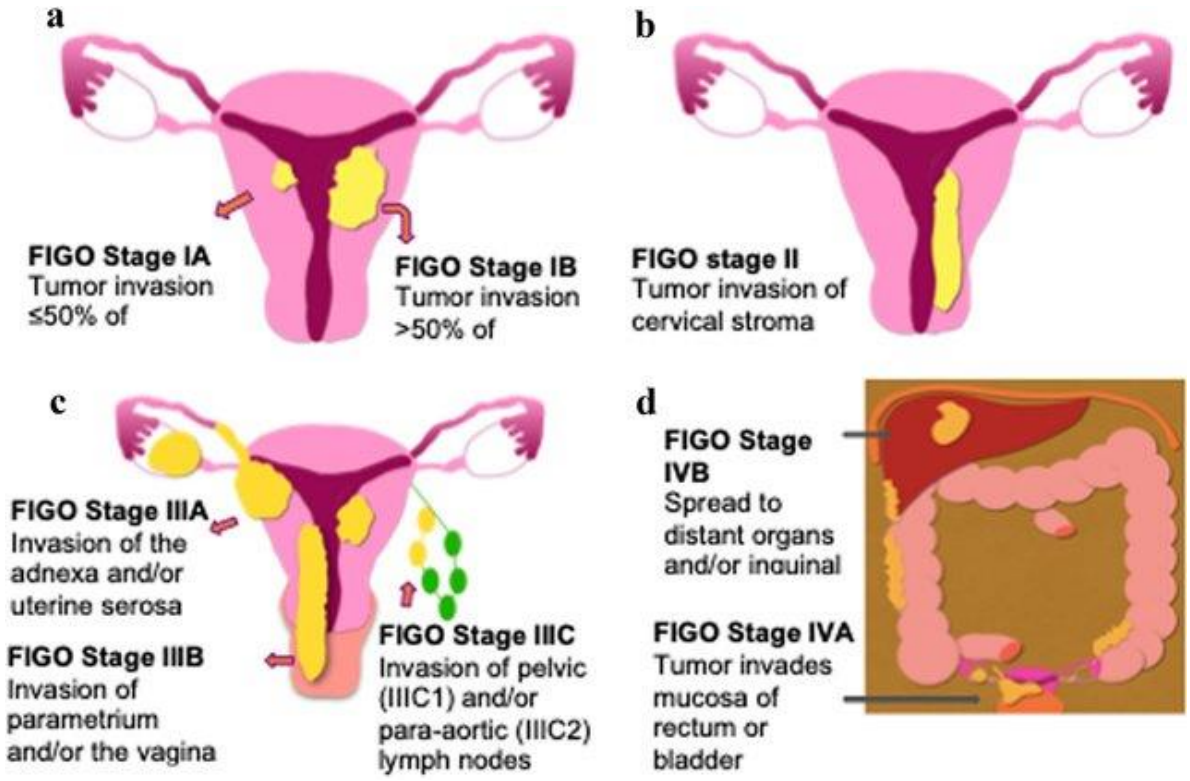


Figure 3: Illustrated FIGO staging system for endometrial Cancer!

TABLE 1 2023 FIGO staging of cancer of the endometrium.[a,b]

Stage	Description
Stage I	Confined to the uterine corpus and ovary[c]
IA	Disease limited to the endometrium OR non-aggressive histological type, i.e. low-grade endometroid, with invasion of less than half of myometrium with no or focal lymphovascular space involvement (LVSI) OR good prognosis disease
	IA1 Non-aggressive histological type limited to an endometrial polyp OR confined to the endometrium
	IA2 Non-aggressive histological types involving less than half of the myometrium with no or focal LVSI
	IA3 Low-grade endometrioid carcinomas limited to the uterus and ovary[c]
IB	Non-aggressive histological types with invasion of half or more of the myometrium, and with no or focal LVSI[d]
IC	Aggressive histological types[e] limited to a polyp or confined to the endometrium
Stage II	Invasion of cervical stroma with extrauterine extension OR with substantial LVSI OR aggressive histological types with myometrial invasion
IIA	Invasion of the cervical stroma of non-aggressive histological types
IIB	Substantial LVSI[d] of non-aggressive histological types
IIC	Aggressive histological types[e] with any myometrial involvement
Stage III	Local and/or regional spread of the tumor of any histological subtype
IIIA	Invasion of uterine serosa, adnexa, or both by direct extension or metastasis
	IIIA1 Spread to ovary or fallopian tube (except when meeting stage IA3 criteria)[c] IIIA2 Involvement of uterine subserosa or spread through the uterine serosa
IIIB	Metastasis or direct spread to the vagina and/or to the parametria or pelvic peritoneum
	IIIB1 Metastasis or direct spread to the vagina and/or the parametria IIIB2 Metastasis to the pelvic peritoneum
IIIC	Metastasis to the pelvic or para-aortic lymph nodes or both[f]
	IIIC1 Metastasis to the pelvic lymph nodes IIIC1i Micrometastasis IIICii Macrometastasis IIIC2 Metastasis to para-aortic lymph nodes up to the renal vessels, with or without metastasis to the pelvic lymph nodes IIIC2i Micrometastasis IIIC2ii Macrometastasis
Stage IV	Spread to the bladder mucosa and/or intestinal mucosa and/or distance metastasis
IVA	Invasion of the bladder mucosa and/or the intestinal/bowel mucosa
IVB	Abdominal peritoneal metastasis beyond the pelvis
IVC	Distant metastasis, including metastasis to any extra- or intra-abdominal lymph nodes above the renal vessels, lungs, liver, brain, or bone

Treatment:

Apart from the standard treatment practices for decade listed above Immune checkpoint inhibitors, a type of immunotherapy, have shown promising outcomes in treating tumours that have defects in a specific DNA repair process, called mismatch repair [17].

On July 31, 2023, the Food and Drug Administration approved Dostarlimab-gxly (Jemperli, GlaxoSmithKline) with carboplatin and paclitaxel, followed by single-agent dostarlimab-gxly, for primary advanced or recurrent endometrial cancer (EC) that is mismatch repair deficient (dMMR), as determined by an FDA-approved test. JEMPERLI injection can be imported by patients or government hospitals only in the name of the patients.

Stage (FIGO Staging Definitions)		Treatment Options
FIGO = International Federation of Gynaecology and Obstetrics		
Stage I and stage II endometrial cancer	Grades 1 and 2	Surgery with or without lymph node sampling
		Postoperative vaginal brachytherapy
		Radiation therapy alone
	Grade 3 (includes serous, clear cell, and carcinosarcoma)	Surgery
		Postoperative chemotherapy with or without radiation therapy
Stage III, stage IV, and recurrent endometrial cancer	Operable disease	Surgery followed by chemotherapy or radiation therapy
	Inoperable disease	Chemotherapy and radiation therapy
	Inoperable disease in which the patient is not a candidate for radiation therapy	Hormone therapy
		Biological therapy

Source: Endometrial Cancer Treatment -Health Professional Version, https://www.cancer.gov/

Treatment Options for Endometrial Cancer

Conclusion:

Endometriosis is a chronic disease associated with severe, life-impacting pain during periods, sexual intercourse, bowel movements and/or urination, chronic pelvic pain, abdominal bloating, nausea, fatigue, and sometimes depression, anxiety, and infertility.

It affects roughly 10% (250 million) of reproductive age women and girls globally. In India endometriosis is estimated to bother about 42 million women in their lifetime.

Epidemiological, biological, and molecular data suggest links between endometriosis and endometrial cancer, with recent epidemiological studies providing evidence for an association between a previous diagnosis of endometriosis and risk of endometrial cancer.

Using the proteomics approach, anti-endometrial antibodies (AEAs - tropomyosin 3 (TPM3), stomatin-like protein2 (SLP-2), and tropomodulin 3 (TMOD3)] were detected in Indian women with endometriosis.

From a pathophysiologic perspective, endometrial carcinomas have been traditionally divided into 2 types: Type 1: includes endometrioid and mucinous carcinoma and Type 2: includes serous, clear cell, undifferentiated carcinoma and carcinosarcoma. Endometrioid histotype constitutes approximately 80% of all endometrial carcinomas, most of which are low grade.

The only way to diagnose womb cancer for sure is to take a sample of the tissue lining the womb (biopsy) and get histopathology report.

Treatment for endometrial cancer usually involves a hysterectomy, salpingo-oopherectomy and adjuvant radiotherapy and/or chemotherapy.

Immune checkpoint inhibitors, a type of immunotherapy, have shown promise in tumours that have defects in a specific DNA repair process, called mismatch repair.

Therefore, all endometriosis cases must be subjected to frozen section endometrial biopsy and the extent of surgery be based on the histopathology, report.

Main challenges for improving EC management include early diagnosis, risk stratification, control of recurrent disease, or more appropriate therapeutic strategies integrating mutational profiles.

Given the public health importance the national and provincial governments must strive to make the diagnostic and treatment facilities in rural areas of developing countries.

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