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Endometriosis

INTRODUCTION

Endometriosis is defined as endometrial glands and stroma that occur outside the uterine cavity

The lesions are typically located in the pelvis but can occur at multiple sites including the bowel, diaphragm, and pleural cavity

While endometriosis is a common and nonmalignant process, ectopic endometrial tissue and resultant inflammation can cause dysmenorrhea, dyspareunia, chronic pain, and infertility.

EPIDEMIOLOGY AND RISK FACTORS

- While the prevalence varies with the population being studied, approximately 10 percent of reproductive-age women globally have endometriosis
- Determining the prevalence of endometriosis in the general population is challenging because some women are asymptomatic, those with symptoms can have varied and nonspecific presentations, and definitive diagnosis typically requires surgery
- In a case-control study of over 5500 women from a national database, the prevalence of endometriosis varied from 1.2 to 1.5 percent, depending upon the inclusion criteria
- When the prevalence of endometriosis was assessed by surgical indication, endometriosis was present in 57 percent of women with endometriosis as a preoperative indication, in 21 percent of women with preoperative pelvic pain, and in 8 percent of women without anticipated endometriosis or pelvic pain.

- actors associated with an increased risk of endometriosis include nulliparity , prolonged exposure to endogenous estrogen (eg, early menarche [before age 11 to 13 years] or late menopause), shorter menstrual cycles (defined as ≤27 days) , heavy menstrual bleeding , obstruction of menstrual outflow (eg, müllerian anomalies), exposure to diethylstilbestrol in utero , height greater than 68 inches , lower body mass index , exposure to severe physical and/or sexual abuse in childhood or adolescence , and a high consumption of trans unsaturated fat
- Factors associated with a decreased risk of endometriosis include multiple births , extended intervals of lactation , and late menarche (after age 14 years) . Increased consumption of long-chain omega-3 fatty acids has been associated with a reduced risk of endometriosis in one prospective study . Race may also be a risk factor, as the prevalence of endometriosis has been reported as being higher in White and Asian women compared with Black and Hispanic women
- . Regarding risk of endometrioma, one retrospective study reported that among women with peritoneal endometriosis, ovarian endometrioma was less common in those women who had used oral contraceptive pills compared with women who had not (18 versus 49 percent) .

CLINICAL MANIFESTATIONS

- **Patient presentation:**
- Women with endometriosis classically present during their reproductive years with pelvic pain (including dysmenorrhea and dyspareunia), infertility, or an ovarian mass
- Women can also present with endometriosis that was incidentally diagnosed during surgery or imaging for other indications
- While the peak prevalence of endometriosis occurs in women 25 to 35 years of age , the disease has been reported in premenarcheal girls and in 2 to 5 percent of postmenopausal women
- In a study of 1000 women with endometriosis, approximately 80 percent presented with pain, 25 percent with infertility, and 20 percent with an endometrioma (ovarian mass). Dysmenorrhea associated with endometriosis is dull or crampy pelvic pain that typically begins one to two days before menses, persists throughout menses, and can continue for several days afterward. Pelvic pain is typically chronic and described as dull, throbbing, sharp, and/or burning . Pelvic pain or pressure are also the most common symptoms associated with an adnexal mass

- The type of endometriosis is suggested by the constellation of symptoms. Examples include
- Women with peritoneal or deeply infiltrating endometriosis often present with dyspareunia. Deeply infiltrating endometriosis lesions can occur on the uterosacral and cardinal ligaments, pouch of Douglas, posterior vaginal fornix, and anterior rectal wall . Introital, or superficial, dyspareunia can result from lesions of the cervix , hymen, perineum , and episiotomy scars
- Women with bladder endometriosis typically present with nonspecific urinary symptoms of frequency, urgency, and pain at micturition . Symptoms can be worsened with menses. Ureteral endometriosis can be asymptomatic or associated with colicky flank pain or gross hematuria
- Women with bowel endometriosis can present with diarrhea, constipation, dyschezia, and bowel cramping. Women with deeply infiltrating endometriosis implants of the posterior cul-de-sac and rectovaginal septum typically present with dyspareunia and painful defecation. Rectal bleeding may occur but is rare

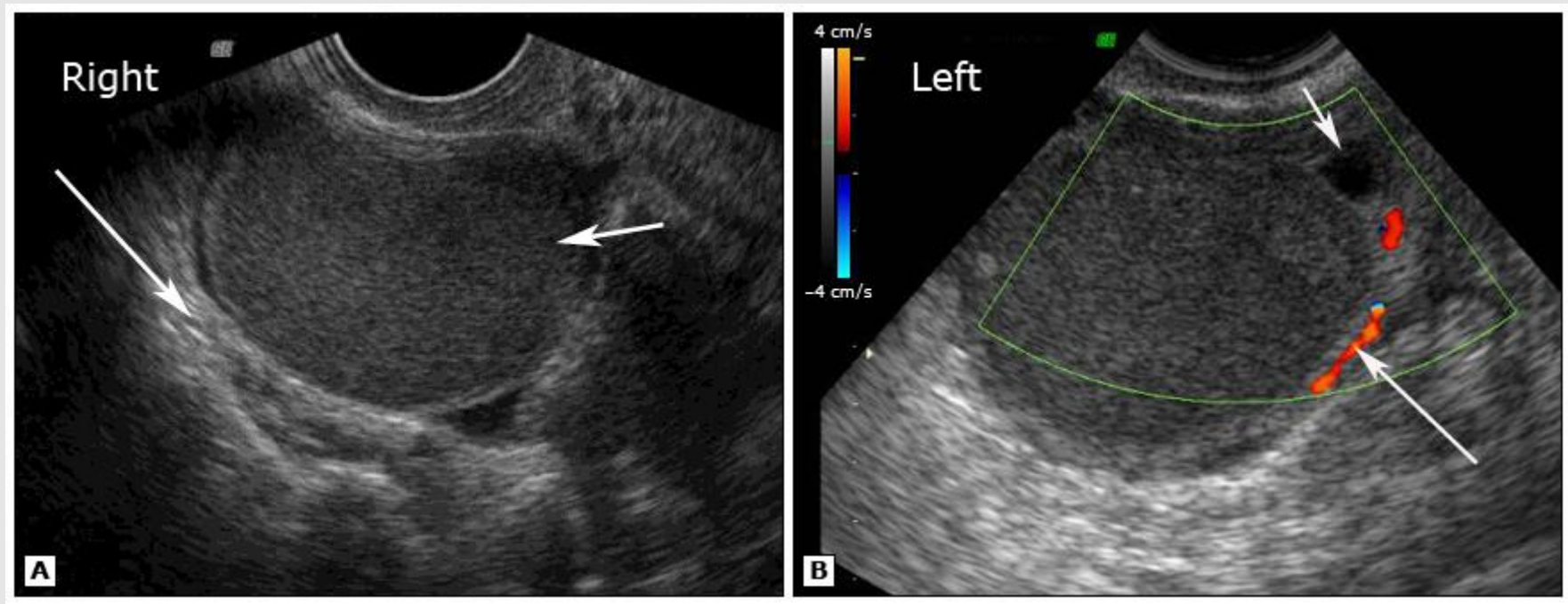
- Women with endometriosis of the abdominal wall typically present with a painful abdominal wall mass; the pain may be cyclic with menses or continuous . Bleeding may also occur. Cyclic bleeding has also been reported with vulvar endometriosis
- **Symptoms:**
- In a national case-control study of over 5500 women with endometriosis, 73 percent of women with endometriosis reported abdominopelvic pain, dysmenorrhea, or heavy menstrual bleeding compared with 20 percent of control women
- A cohort study including over 600 women with endometriosis identified a visceral syndrome of seven symptoms associated with endometriosis that included abdominal pain with no relation to menstruation, pain during urination, pain during defecation, constipation or diarrhea, irregular bleeding, nausea or vomiting, and feeling tired or lacking energy
- The severity of endometriosis does not correlate with the number and severity of symptoms; women with advanced disease may have few or no symptoms and those with minimal or mild disease may have incapacitating pain. **However, in women with deep infiltrating endometriosis, the severity of pain generally correlates with the depth and volume of disease**

- **Physical examination** :
- Physical examination findings in women with endometriosis are variable and depend upon the location and size of the implants.
- Findings suggestive of endometriosis include tenderness on vaginal examination, nodules in the posterior fornix, adnexal masses, and immobility or lateral placement of the cervix or uterus
- Occasionally, speculum examination may reveal characteristic blue-colored implants or red proliferative lesions that bleed on contact, both usually in the posterior fornix
- While physical examination findings are helpful, the examination can also be normal; lack of findings does not exclude the disease. The approach to the pelvic examination is reviewed in detail separately.

- **Laboratory**:
- There are no pathognomonic laboratory findings for endometriosis. While several urinary and endometrial biomarkers have been studied for the noninvasive diagnosis of disease, none are clinically useful.
- CA-125 is a cell surface antigen expressed by derivatives of the coelomic epithelium (including the endometrium) and is well established as a useful marker for the monitoring of women with epithelial ovarian cancer.
- Serum cancer antigen (CA) 125 concentration can be elevated in women with endometriosis (ie, greater than 35 units/mL)
- Although the role of serum CA 125 in primary diagnosis is undefined . However, serum CA 125 concentrations are not routinely ordered in women being evaluated or treated for endometriosis because other diseases, notably ovarian carcinoma, also elevate the serum CA 125 concentration,also during early pregnancy and normal menstruation, and in women with acute pelvic inflammatory disease or leiomyomata. Serum CA-125 concentrations vary somewhat across the menstrual cycle; in general, levels are highest during the menstrual phase and lowest during the midfollicular and periovulatory phases of the cycle

- Overall, the serum CA-125 concentration does not have the necessary sensitivity to be an effective screening test for the diagnosis of endometriosis. Whereas the serum CA-125 generally is not a reliable predictor of the effectiveness of medical therapy, a sustained elevation of serum CA-125 after surgical treatment predicts a relatively poor prognosis.
- Circulating microRNAs: Thousands of miRNAs circulate in the bloodstream and hence offer the possibility to serve as precise biomarkers of disease
- While the mechanism by which miRNA levels are altered is not fully understood, their serum/plasma levels correlate with levels in cancer tissues, suggesting that miRNAs are shed from tissue and released into the circulation. Microarray expression profiling has also demonstrated altered systemic serum miRNA concentrations in women with endometriosis
- Measurement of these miRNAs may represent a novel, noninvasive diagnostic test for early detection and intervention of endometriosis, and is currently under development.

- **Imaging** :
  - Transvaginal ultrasonography can be helpful in identifying women with advanced endometriosis. Transvaginal ultrasonography can detect ovarian endometriomas, but cannot image pelvic adhesions or superficial peritoneal foci of disease.
  - Endometriomas can have varying ultrasonographic features but appear typically as cystic structures with diffuse low-level internal echoes surrounded by a crisp echogenic capsule. Some have internal septations or thickened nodular walls.
  - When the characteristic features are present, transvaginal ultrasonography has 90% or higher sensitivity and almost 100% specificity for detection of endometriomas
  - Transvaginal or transrectal ultrasonography can be especially helpful when deep infiltrating disease involving the bladder, the uterosacral ligaments, or the rectovaginal septum is suspected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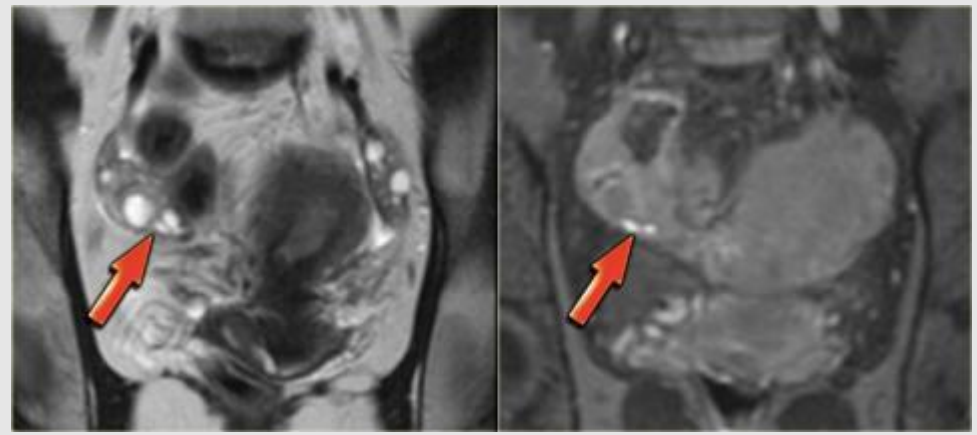
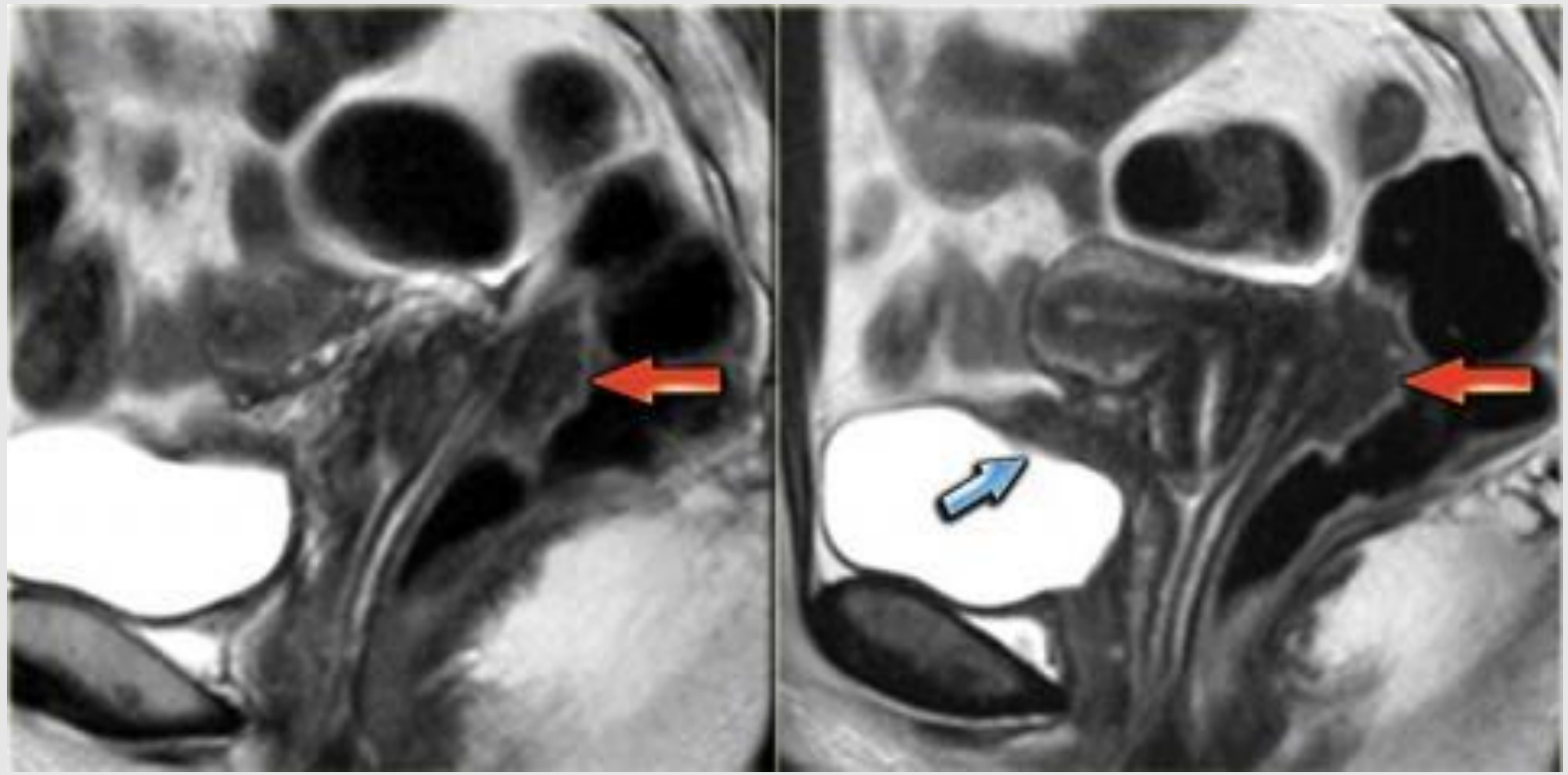
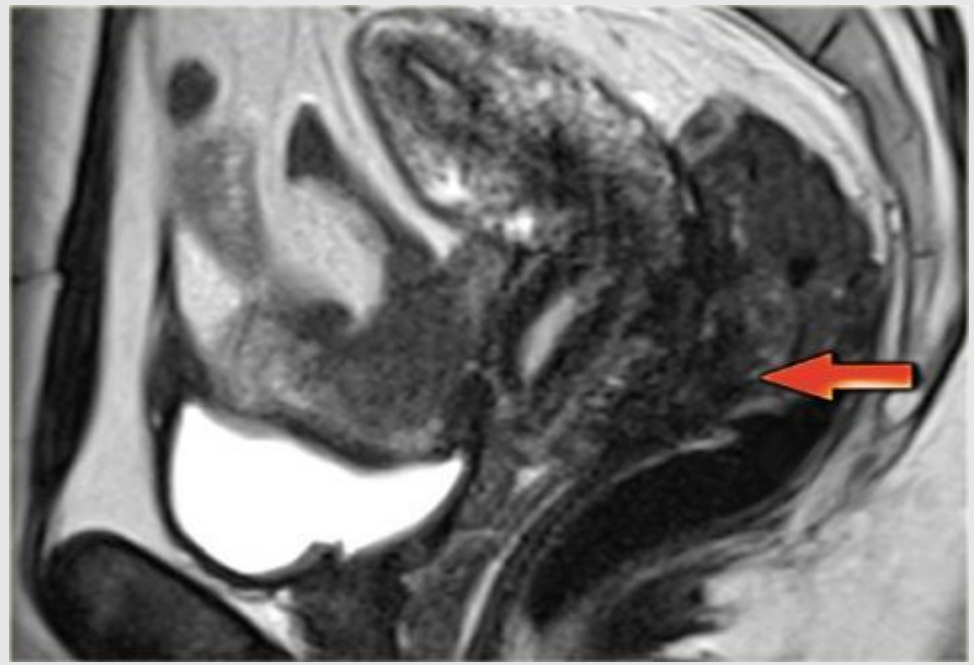


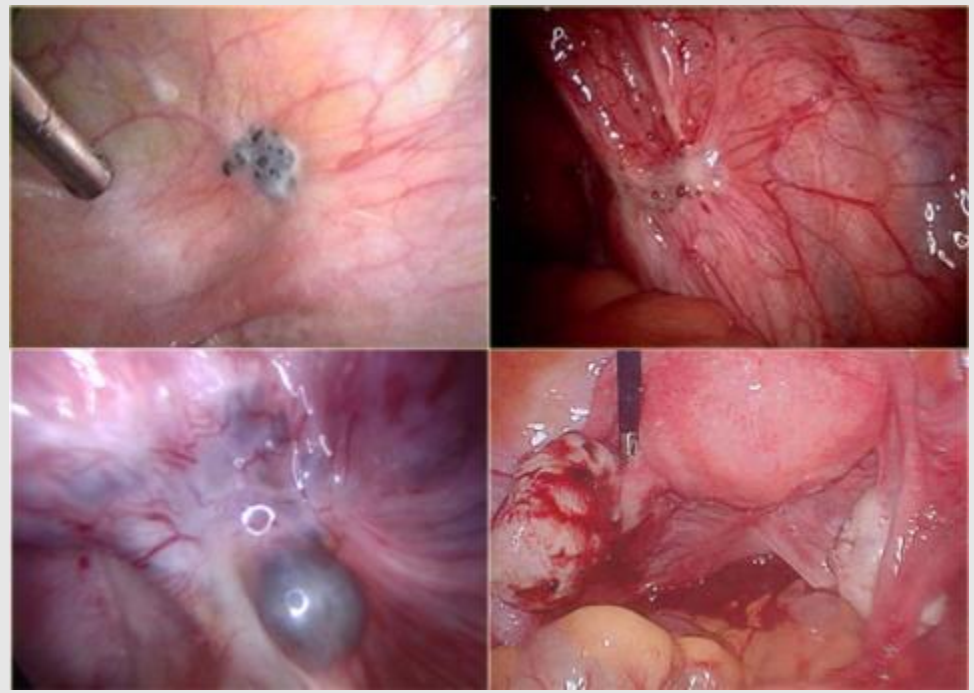




- Like transvaginal ultrasonography, magnetic resonance imaging (MRI) can be helpful in the detection and differentiation of ovarian endometriomas from other cystic ovarian masses, but cannot reliably image small peritoneal lesions
- For detection of peritoneal implants, MRI is superior to transvaginal ultrasonography but still identifies only 30–40% of the lesions observed at surgery. For detection of disease documented by histopathology, MRI is approximately 70% sensitive and 75% specific.
- The principal advantage MRI has over ultrasonography is its ability to distinguish more reliably between acute hemorrhage and degenerated blood products. Whereas endometriomas usually exhibit a relatively homogeneous high signal intensity on T1-weighted images and a hypointense signal on T2-weighted images (“shading”), acute hemorrhage generally has low signal intensity on both T1- and T2-weighted images.

- However, an interval 6-week observation, during which hemorrhagic cysts will typically regress, followed by repeat TVUS accomplishes the same goal. Gadolinium contrast offers no additional diagnostic value. MRI also can be used to aid in the diagnosis of deep infiltrating and rectovaginal disease. Neither ultrasound nor MRI can be used to rule out endometriosis.

- **DIAGNOSIS:**
- **Definitive diagnosis** — Endometriosis is definitively diagnosed by histologic evaluation of a lesion biopsied during surgery (typically laparoscopy)
- While visual confirmation of endometriosis without biopsy is considered diagnostic by some experts, visual confirmation alone is of limited value because the accuracy is impacted by the surgeon's expertise
- Definitive diagnosis of endometriosis is often delayed because the symptoms of endometriosis are vague, the symptoms overlap with a number of gynecologic and gastrointestinal processes, and a surgical diagnosis entails risk. Studies have reported an average diagnostic delay of 7 to 12 years in women with endometriosis.



- **Role of presumptive diagnosis:**
- While definitive diagnosis requires tissue biopsy and histologic confirmation, the combination of symptoms, signs, and imaging findings can be used to make a presumptive, nonsurgical diagnosis of endometriosis
- . A clinical diagnosis can be sufficient to initiate therapy that is low risk and easily tolerated (eg, estrogen-progestin contraceptives in women who are not trying to conceive). However, the presence or absence of a response to empiric treatment cannot be construed as definitive confirmation or exclusion of the diagnosis

- **Nonsurgical diagnosis** — Possible options for non-surgical diagnosis include clinical diagnosis based upon examination and imaging findings or serum diagnosis using microRNA markers.
- A nonsurgical diagnosis of endometriosis includes: (1) ultrasonographic finding of ovarian endometrioma, (2) visual inspection of the posterior vaginal fornix and biopsy of rectovaginal lesions, (3) cystoscopic evaluation and biopsy of detrusor lesions, and (4) physical examination findings of rectovaginal endometriosis that are confirmed with imaging . Although this approach does not require laparoscopy, tissue biopsy can still provide a definitive diagnosis while imaging findings make the diagnosis highly likely. Of note, this approach is useful only for clinicians with significant skill in the examination, sonography, and cystoscopy of women with endometriosis.


THANK YOU