



# Endometriosis in adolescents: a narrative review

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**Background and Objective:** Endometriosis is a gynecologic disease commonly presenting as chronic pelvic pain (CPP) and can occur in adolescents. The exact pathogenesis is unknown, but several risk factors have been well identified. History and physical examination may provide clues in considering endometriosis, but the definitive diagnosis is surgically determined by performing a laparoscopy. There are different treatment modalities established with the main goal of controlling pain and preventing future complications such as infertility.

**Methods:** An electronic search was performed on MEDLINE and PubMed to identify relevant articles from 1980 to 2019.

**Key Content and Findings:** This narrative review focuses on pelvic pain particularly endometriosis and the best practical approach in evaluating and managing affected adolescent females.

**Conclusions:** Diagnosis of endometriosis is possible in young females presenting with chronic pelvic pain. Recognition of its prevalence and risk factors increases suspicion so as not to delay diagnosis. Management entails use of appropriate analgesics and consideration for hormonal interventions. Laparoscopy is both diagnostic and therapeutic, and helpful in prevention of future complications.

**Keywords:** Adolescent; dysmenorrhea; endometriosis; pelvic pain

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## Introduction

Pelvic pain related to menstruation refers to dysmenorrhea. It is the most common menstrual symptom reported among adolescents and is the leading cause of school absences among adolescent females (1). Dysmenorrheal episodes are usually due to primary causes, but not uncommonly, secondary causes such as endometriosis can occur. Endometriosis causes chronic pelvic pain (CPP) and dysmenorrhea in women of reproductive age (2). This article will review the prevalence, pathogenesis, and risk factors of endometriosis, as well as discuss the evaluation, current treatment approaches, and complications related to untreated endometriosis.

## Methods

A literature search was performed on the electronic databases including MEDLINE and PubMed, from 1980 to 2019, to identify all relevant studies and reviews. A combination of the search terms included “pelvic pain, dysmenorrhea, endometriosis, and adolescent”. The reference list also included studies identified manually, and studies referenced for other purposes.

## Dysmenorrhea and CPP

Dysmenorrhea is defined as menstrual pain and is separated into primary and secondary causes (3). Primary

dysmenorrhea is painful menstruation without underlying pelvic pathology (4). The majority of dysmenorrhea in adolescent girls is primary in etiology, which is common within 6 to 12 months post-menarche (3). Primary dysmenorrhea is usually responsive to treatment with oral contraceptive pills (OCPs) or nonsteroidal anti-inflammatory drugs (NSAIDs) (3). Secondary dysmenorrhea includes underlying pathology of the uterus, and endometriosis is the most common form of secondary causes found in adolescents (3,4).

CPP is defined as pain in the pelvic region that lasts for at least 6 months, and can be cyclical, noncyclical, constant, or intermittent (3). Laufer *et al.* found approximately 70% prevalence of endometriosis in adolescent females with CPP resistant to treatment. Classically, cyclic pain is associated with adult endometriosis, whereas adolescents with endometriosis are more likely to present with noncyclical pain (5).

### Prevalence of endometriosis

Endometriosis affects 6% to 10% of women of reproductive age (6). The exact prevalence of adolescent endometriosis is difficult to determine due to the invasive method of definitive diagnosis of endometriosis via laparoscopy and the absence of large-scale studies within this population. Approximately 60% of adult women with endometriosis experience symptoms prior to the age of 20 (2).

Janssen *et al.* published a systematic review of literature from 1980–2011 to determine the prevalence of endometriosis in adolescents with dysmenorrhea or CPP (7). From their literature search, 15 articles met their search criteria, with 880 adolescent girls with CPP or dysmenorrhea being included in their analysis. Almost two thirds (62%) of the compiled population had laparoscopic evidence of endometriosis (range, 25–100%). Endometriosis was present in 75% of adolescents with CPP resistant to treatment with OCPs or NSAIDs, and 49% of girls with CPP not resistant to treatment, as well as 70% of adolescent girls with dysmenorrhea. This study was limited by the retrospective nature of 9 out of 15 of the studies used, hence there may have been an overestimation of the prevalence of endometriosis in this population (7).

Furthermore, the definition of CPP was not stated in the published articles, therefore the threshold for laparoscopy could have significant variation between studies. Large scale studies with unified threshold for laparoscopy in adolescent

populations with dysmenorrhea or CPP are needed to determine the prevalence of endometriosis in teenagers.

### Pathophysiology

Endometriosis is a multifactorial condition with the exact pathophysiology that is not fully understood (8). There is no current unifying theory in the occurrence of endometriosis. The true pathogenesis of endometriosis may have a component of many of the current postulated theories. There are three proposed mechanisms that are generally accepted: direct implantation via retrograde menstruation, lymphatic and vascular dissemination of endometrial cells, and coelomic metaplasia.

The most widely accepted theory is the direct implantation theory (Sampson theory), viable endometrial cells relocate via retrograde menstruation through the fallopian tubes into the peritoneum leading to direct implantation of endometrial tissue outside of the uterus (9). However, the majority of healthy women have retrograde menstruation, but only 10% develop endometriosis (10). There may be a component of immune dysfunction in women with endometriosis that interferes with the clearance of the lesions that have relocated via retrograde menstruation (6). Other theories of the cause of retrograde menstruation leading to endometriosis include a genetic predisposition, progesterone resistance, estrogen dependence, and inflammation (10). Lymphatic and vascular dissemination of endometrial cells has been postulated, and this theory would account for extra peritoneal locations of endometriosis such as lymph nodes, the pleural cavity, brain, and kidney (11).

The coelomic metaplasia theory suggests metaplasia of coelomic epithelium covering the peritoneum and ovary can lead to pelvic endometriosis, immunological or hormonal factors are thought to stimulate this transformation (12,13). Coelomic metaplasia may account for the development of endometriosis in prepubertal girls and adolescents with severe variants (8).

There are other proposed mechanisms that could contribute to endometriosis including estrogen driven proliferation of endometrial lesions, oxidative stress, and inflammation leading to recruitment of inflammatory mediators that promote growth of endometrial lesions, suppression of apoptosis promoting survival of endometrial cells, and stem cells differentiating into endometrial cells outside of the uterus (8).

## Risk factors

There are many risk factors associated with endometriosis in adolescents including genetic, anatomic, and hormonal factors. There is a genetic link to endometriosis in adolescents, as seen with adult patients. A recent retrospective study found a positive family history in a third of cases, with a first-degree relative affected in a quarter of cases of adolescents with surgically confirmed endometriosis (14).

Obstructive Mullerian anomalies can lead to increased retrograde menstruation and have been shown to increase the risk for endometriosis in adolescents (2). This is supported by the finding of spontaneous resolution of endometriosis in adolescent patients after the obstruction is surgically corrected (15,16).

Early age of menarche is associated with higher risk of endometriosis due to increased exposure to estrogen and increased duration of retrograde menstruation (17). Early onset of dysmenorrhea and CPP at the time of menarche increases the probability of having endometriosis (16,18). Low BMI has been shown to be correlated with increased risk of endometriosis (17).

## Diagnosis

Clinical presentation in adolescents can be suggestive of endometriosis, physical examination can be useful in certain situations, but definitive diagnosis requires invasive laparoscopy procedure. The clinical presentation of endometriosis is variable and the definitive diagnosis of endometriosis requires direct visualization via laparoscopy and histological characterization (8). There is often a significant lag between the onset of symptoms and diagnosis (19).

The presence of symptoms of dysmenorrhea or CPP resistant to therapy should raise concern for endometriosis (2). Nausea accompanying pain is a common presentation in adolescents (19). Gastrointestinal symptoms such as constipation, dyschezia, and intestinal cramping may be experienced (2). If the adolescent is sexually active, dyspareunia may be present (2).

Vaginal examination may show retroverted uterus with limited mobility, however a vaginal exam may be inappropriate in the case of a non-sexually active adolescent (20). A rectal examination may reveal tender uterosacral ligament with rectovaginal nodules (20).

Pelvic ultrasound can detect ovarian endometriomas, however it is not sensitive in detecting superficial

endometriosis (20). A normal ultrasound does not rule out endometriosis, and the gold standard for diagnosis is laparoscopy.

Diagnostic laparoscopy with histological characterization of biopsy specimens is used in adolescents to diagnose endometriosis and can be used as a treatment (2). If medical management of symptoms has failed in the adolescent patient it may be reasonable to consider proceeding with laparoscopy, however there is no consensus on this issue (2). Staging of endometriosis is classified by the Revised American Society for Reproductive Medicine (rASRM) scoring system based on the appearance, location, type, and depth of invasion of the lesion (21). The rASRM disease staging ranges from I, indicating mild/early endometriosis, to IV, indicating severe/advanced endometriosis (21). *Table 1* shows the different staging described for endometriosis.

The rASRM system is used to determine disease burden, but does not correlate with pain severity or responsiveness to treatment. There is large variability in the rASRM staging in adolescents. Earlier studies found that majority of adolescents were diagnosed with early stage endometriosis (rASRM stage I or II), though more recent studies have shown a prevalence of advanced stage endometriosis (rASRM stage III or IV) (2). Adolescent endometriosis lesions have a different laparoscopic appearance as compared to adult endometriosis lesions. Adolescent endometriotic lesions appear red or clear/vesicular and may be difficult to see, as compared to adult endometriotic lesions which are classically described as “powder burn” lesions which are black with white scarring (2). Red and clear lesions have increased metabolic activity resulting in increased prostaglandin production manifesting as substantial pain (3).

## Management

The importance of treating endometriosis in adolescents is two-fold: control of symptoms and prevention of disease progression, which may decrease long-term consequences such as infertility (22). Management can be sought after with non-hormonal therapy, hormonal therapy, or surgical excision and destruction of any visual evidence of endometriosis (23).

The standard evaluation of pelvic pain in adults generally begins after 6 months of continued pain while on OCPs and/or NSAIDs. However, waiting 6 months for proper evaluation and treatment in adolescents can lead to patients missing school and other school activities. Thus,

**Table 1** Staging in endometriosis

Stage	Description	Points	Characterization
1	Minimal	1–5	Few small implants, wounds, or lesions
2	Mild	6–15	More implants, deeper into the tissue, with/without scarring
3	Moderate	16–40	Deep implants with small cysts (chocolate cysts) seen in both ovaries; presence of scarring tissue
4	Severe	>40	Widespread distribution with larger cysts in both ovaries; thicker scarring tissue

initiation of treatment can be started on any postmenarchal adolescent, and further assessment is warranted if dysmenorrhea continues after 2 or 3 cycles of OCP use (24).

First line management is medical therapy using OCP and NSAIDs due to their effectiveness, safety, cost profile, and general toleration by patients (23). Hormonal therapy aims to suppress the production of ovarian estradiol therefore decreasing endometriotic growth and proliferation, and inducing atrophy and/or decidualization (25). Non-hormonal therapies such as NSAIDs, tricyclic antidepressants, and off label use of gabapentin can be used in conjunction with hormonal therapy to decrease pelvic inflammation and pain (25). Some affected individuals resort to homeopathic and nutritional alternatives.

Due to the routine scenario of adolescent patients being noncompliant with medical treatment, Levonorgestrel intrauterine device should be considered. Levonorgestrel IUD delivers 20 micrograms per day over 5 years, not needing repeat administration. The levonorgestrel causes atrophy and pseudodecidualization to the uterine lining, along with apoptosis of endometrial glands and stroma (26). This is demonstrated with improvement in bleeding patterns and amenorrhea, which can be used as evidence of treatment efficacy because endometrial suppression can be interpreted as a sign of ectopic endometrial suppression (26).

Surgical therapy for endometriosis is typically necessary for intractable pelvic pain despite medical therapy (23). The surgical treatment should be performed during the diagnostic laparoscopy (14).

### Complications

Unger *et al.* explained in a case series of three adolescents, aged 13–16 with laparoscopic diagnosis of stage 1 endometriosis who were noncompliant with postoperative medical management and demonstrated disease progression on their second laparoscopy (27). The combination of

surgical-medical approach significantly prevents disease progression and can lead to protection of patients' fertility (27). Unfortunately, long-term management concerns for adolescents are still debated due to lack of consistent data, and the need for prospective studies to assess recurrences of symptoms, disease progression, reoperation rates, and impact on subsequent fertility (14).

Recurrence of the disease depends on multiple influences; type of initial lesions, treatment used, length of follow up, and criteria for diagnosis (14). Audebert *et al.* had performed a retrospective cohort study on 55 patients, ages 12–19, who were diagnosed with endometriosis from March 1998 to April 2013. Of these 55 patients, 18 patient desired pregnancy, and 72.2% achieved successful live birth. Nine of the thirteen pregnancies occurred in patients with stage I or II endometriosis. In total, 54.5% of the eleven subfertile patients had delivered a child, 2 of which used *in vitro* fertilization (IVF) (14). According to ACOG, if initial surgery endometriosis-associated infertility is unsuccessful, IVF should be performed rather than reoperation, since repetitive ovarian surgery has been shown to have negative impact on IVF (3).

### Conclusions

A menstruating adolescent complaining of dysmenorrhea should not be disregarded especially if the clinical presentation is suggestive of secondary causes. Endometriosis can be present in young females and commonly presents as CPP. Recognition of its prevalence and risk factors increases suspicion so as not to delay diagnosis. If indicated, a laparoscopic approach can be both diagnostic and therapeutic, particularly in cases that the recommended stepwise approach of analgesics and hormonal interventions lack provision of relief. Adolescent females with endometriosis should not be deprived of having good quality of life and should not suffer the complications of infertility.

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