INDIAN FERTILITY SOCIETY

SIG Newsletter

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SIG Endometriosis

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Endometriosis in Adolescents

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Endometriosis has an impact on about 10% of pre-menopausal women worldwide. The exact prevalence of this condition in adolescents is still unknown. Onset of clinical symptoms like dysmenorrhea occurs after menarche, but diagnosis is often delayed by few years.

Many girls experience dysmenorrhea during their teenage years which seriously disorganizes daily activities, school performance and regular rest as well as psychological welfare. Dysmenorrhea can be classified into primary (without the organic disease) and secondary (attributable to organic pathology in pelvic area).[1] The fact that adolescents' dysmenorrhea is frequently considered a normal part of menstruation, it brings about

inadequate recognition for this symptom before mismanagement occurs due to endometriosis. This means that there should be more awareness raised for these particular people and proactively managed with regard to handling special challenges they face here.

Primary and Secondary Dysmenorrhea

Primary dysmenorrhea is the most common menstrual symptom among adolescents and young women. It is described as recurrent lower abdominal pain during menstruation as is often the primary complaint. Although this pain is typically defined as mild to moderate, it significantly reduces quality of life and remains underreported. The prevalence of primary dysmenorrhea in adolescents ranges from 45% to 95%, but it is still underestimated since many women do not seek medical advice for the same.[2]

Primary dysmenorrhea usually begins within 6–12 months after menarche and with the pain often starting just before menses. This pain is due to the elevated prostaglandin levels, which cause myometrial hypercontractility, leading to uterine muscle hypoxia, ischemia, and pain, along with systemic symptoms like nausea, diarrhea, and fatigue.

For pre-sexually active adolescents and young women having symptoms of primary dysmenorrhea without other endometriosis symptoms, empirical medical treatment is recommended to ease the pain. However, if symptoms persist despite treatment, further evaluation is necessary to exclude secondary causes, including pelvic examination and imaging.

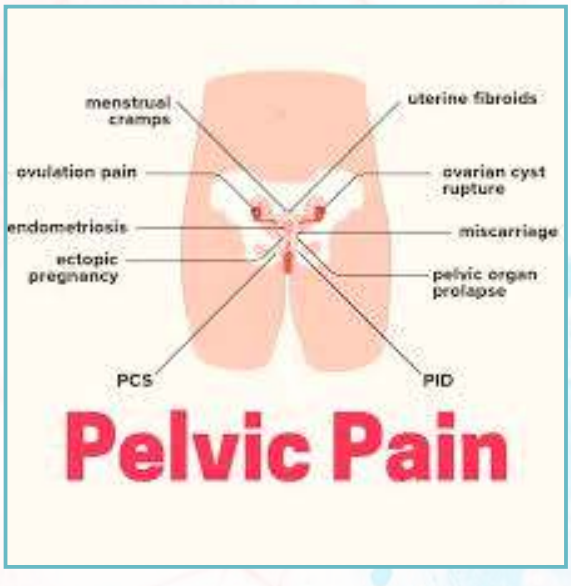


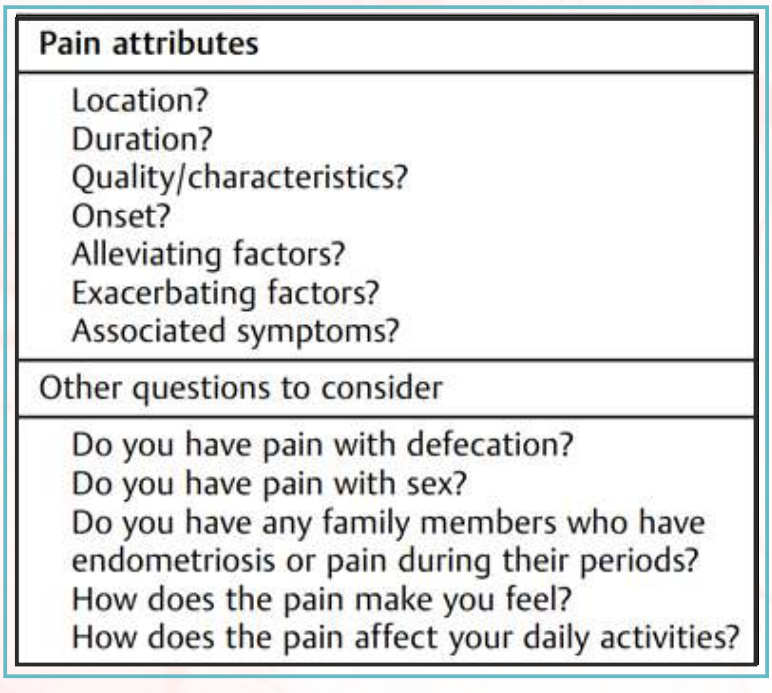
Figure 1 : Pelvic Pain

Secondary dysmenorrhea is characterized by the presence of menstrual pain associated with organic disease, which can either be due to gynaecological or non-gynaecological causes. The gynaecological aetiologies commonly include endometriosis, adenomyosis, fibroids, postoperative adhesion syndrome, pelvic inflammatory disease (PID), ovarian cysts, hematocolpus due to obstructive Müllerian abnormalities, and hydrosalpinx. Where as the non-gynaecological origins often encompass gastrointestinal and urinary tract diseases.

Gynecologic	Urologic	Gastrointestinal	Musculoskeletal
Dyspareunia Vaginitis Vestibulitis Vulvodynia Endometriosis Adenomyosis	Interstitial cystitis Urethral diverticulum Urolithiasis Radiation cystitis Malignancy	Constipation Irritable bowel syndrome Inflammatory bowel disease Diverticular disease Enterocolitis Malignancy Hernia	Pelvic floor dysfunction Myofascial pain

Figure 2 : Differential diagnosis for pelvic pain

A comprehensive evaluation of secondary dysmenorrhea necessitates a multidisciplinary approach. This begins with a meticulous medical history that assesses every aspect of menstruation like onset of menarche, duration of bleeding, menstrual cycle intervals, and menstrual flow volume in the form of potentially quantified using a pictorial blood loss assessment chart (PBAC). Detailed history should be taken which includes intensity of pain, nausea, diarrhoea, and fatigue, along with the timing, intensity, and the impact of these symptoms on daily activities.



Pain attributes
Location? Duration? Quality/characteristics? Onset? Alleviating factors? Exacerbating factors? Associated symptoms?
Other questions to consider
Do you have pain with defecation? Do you have pain with sex? Do you have any family members who have endometriosis or pain during their periods? How does the pain make you feel? How does the pain affect your daily activities?

Figure 3 : Questions to ask adolescent in history taking?

Blood investigations, should include a complete blood count, C-reactive protein levels, metabolic panel, and urinalysis with culture. If there are bowel symptoms, it is crucial to consider gastrointestinal problems. Other evaluations include for growth delay, weight loss, bloody diarrhoea, faecal calprotectin levels, circulating antibodies against tissue transglutaminase, and HLA typing which can help reach a diagnosis.

An endoscopic examination may be required to differentiate between various pathologies.
Bowel involvement in endometriosis ranges from 2% to 46%, with lower rates in adolescents.[3] Similar symptoms can arise from conditions like Irritable Bowel Syndrome (IBS), inflammatory bowel diseases (IBD), and celiac disease. IBS is notably more common in females with endometriosis.

IBD affects about 20% of children and adolescents, often delaying puberty and causing growth issues, weight loss, and bloody diarrhea.[4] Fecal calprotectin is an useful tool for screening, but the confirmatory diagnosis is through endoscopic assessment along with biopsies. Radiological imaging helps in identifying Crohn's disease involvement in the small or proximal large intestine.

Celiac disease affects 1% to 3% of Caucasian adolescents,[5] with over 40% presenting gastrointestinal symptoms and conditions like hypothyroidism, diabetes, and delayed menarche.[6] Diagnosis often involves detecting circulating antibodies against tissue transglutaminase, with HLA typing aiding in diagnosis.
The less common causes of intestinal symptoms include Meckel's diverticulum and subacute/chronic appendicitis. Congenital uterine anomalies also warrant consideration since they also present with pain and abnormal bleeding at menarche. Pelvic ultrasound and MRI are essential for evaluating these anomalies.

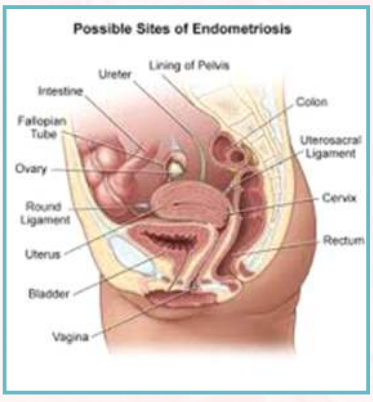


Figure 4 : Possible sites of endometriosis

In adolescents along with these symptoms, a thorough pelvic assessment is crucial, despite potential challenges. A multidisciplinary approach ensures accurate diagnosis and effective treatment, addressing the complex interplay of symptoms and underlying causes in suspected endometriosis and related disorders

Diagnosis

For adolescents presenting with dysmenorrhea, a thorough evaluation is essential to rule out endometriosis and any other underlying conditions. This begins with an accurate medical history to determine the age of first menstruation, menstrual cycle characteristics, prior surgical treatments, autoimmune and endocrinological diseases, and family history of endometriosis. It's also critical to assess medication use, particularly NSAIDs and estro-progestin therapy, to gauge symptom severity.

Following the ESHRE guidelines, clinicians should investigate other conditions related to endometriosis, such as early menarche, family history, persistent pain despite treatment, heavy menstrual bleeding, and gastrointestinal or genitourinary symptoms.[7] Nausea, fatigue, and the impact on daily activities should also be noted.

The next step involves a physical examination, which may include vaginal and/or rectal exams. These exams should be discussed with the adolescent and their caregiver, considering their acceptability based on age and cultural background. In cases where a physical examination is appropriate, it should be performed carefully to minimize discomfort.

Instrumental evaluation is crucial, with ultrasound and MRI being the primary imaging techniques. Given the constraints of ultrasound in pre-sexually active adolescents, a transabdominal or transrectal approach is recommended.

Figure 5 : Ultrasound features showing ground glass appearance of endometriotic cyst

If there is clinical suspicion of posterior compartment involvement then transrectal ultrasound is a viable alternative, for detecting deep infiltrating endometriosis (DIE).

MRI is a non-invasive technique with high diagnostic accuracy and should be considered when ultrasound results are inconclusive or when patients object to transrectal evaluation. MRI is particularly useful for identifying anterior and posterior endometriosis and differentiating between superficial ovarian implants and endometriotic cysts.

Serum biomarkers like CA-125 are not recommended for diagnosing endometriosis in adolescents or premenopausal women due to their lack of specificity. Future advancements may identify more accurate biomarkers related to the inflammatory and autoimmune aspects of endometriosis.[8]

Surgical confirmation of endometriosis is generally considered inappropriate for both adolescents and adults according to ESHRE recommendations. Instead, non-invasive diagnostic approaches and careful clinical examination should guide the management of suspected endometriosis in adolescents.

Management

The primary aim of medical therapy for adolescents and young women with endometriosis is to alleviate painful symptoms, prevent its progression , and protect future fertility. The ESRHE guidelines recommend treating endometriosis-related pain in adolescent girls with hormonal contraceptives or progestins. However, there is no consensus on the best therapy for different ages and patient types given the variability of endometriosis features.[7]

Progestin therapy, like Dienogest and Norethindrone acetate, are effective and well-tolerated. Dienogest, helps to reduce pain, improving quality of life, and decreasing the size and vascularization of endometriotic lesions through its progestogenic and antiestrogenic effects. However, side effects such as estrogen deprivation symptoms can occur, necessitating a switch to estro-progestin therapy in some cases. For dysmenorrhea, oral contraceptives are more effective when used continuously rather cyclically.
For women who cannot tolerate oral administration, a subcutaneous implant of etonogestrel (ENG) or the LNG-IUS device might be viable alternatives. GnRH agonists are reserved as a second-line treatment for adolescents with confirmed endometriosis unresponsive to other therapies, and should be coupled with add-back therapy to mitigate side effects like bone density loss.
Emerging therapies, such as Ankaferd Blood Stopper (ABS) and oxytocin, show promising results in reducing endometriosis progression. Ankaferd Blood Stopper (ABS) is a hemostatic agent made from a blend of traditional plant extracts. It includes a standardized mix of Thymus vulgaris, Glycyrrhiza glabra, Vitis vinifera, Alpinia officinarum, and Urtica dioica. ABS has pleiotropic effects, which includes antineoplastic, anti-microbial, anti-mutagenic, antioxidant, and tissue-healing properties, although the acting mechanisms is still under research, it has been reported that it may induce the formation of erythrocyte aggregation in the place of bleeding, and it works as a haemostatic agent providing a therapeutic effect on endometriosis foci. [7]

For adolescent endometriosis, treatment plan should be individualized.

Surgery is considered only in specific conditions, focusing on preserving fertility and hormonal function. Indications for surgical intervention include rapid growth of an ovarian endometriotic cyst, suspicious ovarian cysts where malignancy cannot be excluded, persistent pain despite hormonal treatment, or urinary and bowel complications.[7]

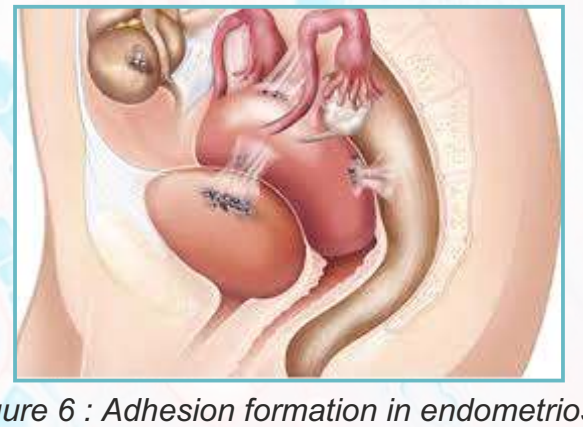


Figure 6 : Adhesion formation in endometriosis

During surgery, minimizing damage to the healthy tissue and preserving ovarian reserve is critical. Techniques such as the stripping technique and CO2 laser vaporization are preferred for their efficacy and minimal recurrence rates.[9] It is important to carefully identify and excise small endometriotic lesions, which are often difficult to detect.

Adolescents and young women often experience higher recurrence rates of endometriosis post-surgery compared to premenopausal women, likely due to higher plasma estrogen levels or a more aggressive disease form. Postoperative recurrence of ovarian cysts and pain symptoms occurs in 40-50% of cases within five years in those not on hormonal therapy. Therefore, continued medical treatment post-surgery is recommended to prevent recurrence and reduce the need for additional surgeries. [10]

In severe cases unresponsive to medical treatment, surgical intervention may be necessary to restore anatomy and improve quality of life, despite the associated risks and side effects.

In adolescents with severe dysmenorrhea and/or endometriosis-associated pain, clinicians should prescribe hormonal contraceptives or progestogens (systemically or via LNG-IUS) as first line hormone therapy because they may be effective and safe. However, it is important to note that some progestogens may decrease bone mineral density.	⊕○○○
The GDG recommends clinicians consider NSAIDs as treatment for endometriosis-associated pain in adolescents with (suspected) endometriosis, especially if first line hormone treatment is not an option.	GPP
In adolescents with laparoscopically confirmed endometriosis and associated pain in whom hormonal contraceptives or progestogen therapy failed, clinicians may consider prescribing GnRH agonists for up to 1 year, as they are effective and safe when combined with add-back therapy.	⊕⊕○○
The GDG recommends that in young women and adolescents, if GnRH agonist treatment is considered, it should be used only after careful consideration and discussion of potential side effects and potential long-term health risks with a practitioner in a secondary or tertiary care setting.	GPP

Figure 7 : The recommended diagnostic process for endometriosis.
DE, Deep Endometriosis; US, Ultrasound

Conclusion

In summary, managing endometriosis in adolescents requires a careful balance of medical and surgical interventions tailored to individual needs, with a strong emphasis on preserving future fertility and minimizing long-term health impacts.

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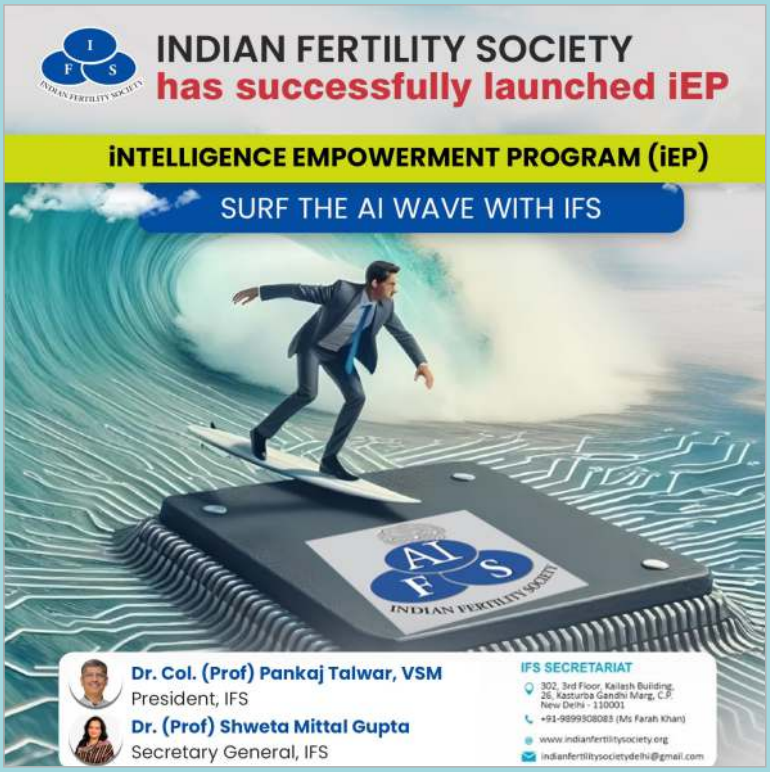
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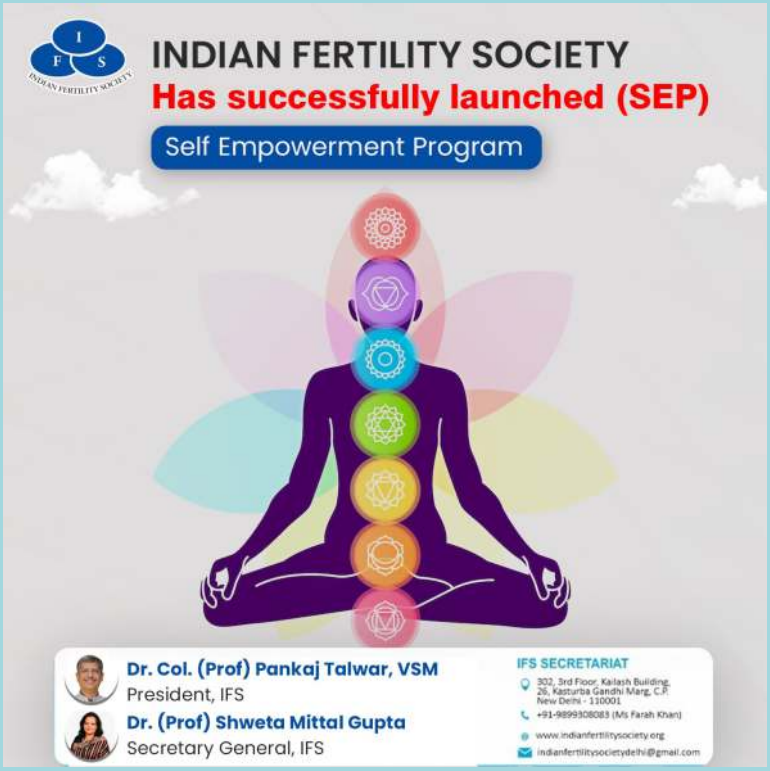
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