

Special Report

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Endometriosis in teenagers

Endometriosis affects a significant proportion of teenagers. Published studies suggest that laparoscopically confirmed endometriosis could be found in over 60% of adolescent girls undergoing laparoscopic investigation for pain, in 75% of girls with chronic pelvic pain resistant to treatment and in 70% of girls with dysmenorrhea and in approximately 50% of girls with chronic pelvic pain not necessarily resistant to treatment. Both early and advanced forms, including deep endometriosis have been reported to be present in teenagers. It has recently been claimed that deep endometriosis has its roots in teenage years. Risk factors include obstructive müllerian anomalies, family history, early menarche and early onset dysmenorrhea. Both surgical and medical treatment approaches are used for treatment in this age group, but care should be taken when treatment with GnRHa and progestins is being considered due to their potential impact on bone formation. Further studies are urgently needed to determine whether early diagnosis and treatment of teenage endometriosis lead to better long term outcomes or simply increase number of interventions without preventing progression of the disease.

Keywords: adolescent endometriosis • combined oral contraceptives • deep endometriosis • depomedroxyprogesterone acetate • laparoscopic surgery • peritoneal endometriosis • primary dysmenorrhea • secondary dysmenorrhea • superficial endometriosis • teenage endometriosis

Endometriosis was once thought to occur rarely in teenagers and was presumed to affect women in later reproductive years. However, with increasing awareness both among the healthcare professionals and general population, it is now well established that endometriosis affects a significant proportion of teenagers. This is reflected in the number of publications included in the PubMed; a search with the keyword 'adolescent endometriosis' reveals less than ten publications per year on average before 1980, whereas this figure is over 70 after 2010.

However, delayed diagnosis is still a major problem and continues to result in a lack of appropriate treatment for the symptoms this condition can cause. Pain symptoms of endometriosis cause suffering and are responsible

for a significant level of absence from school and limitation of activity.

Prevalence

Dysmenorrhea is a common symptom in teenagers and affects up to 40–50% of young women, with severe forms in 15% [1]. Painful periods in teenagers are usually due to primary dysmenorrhea (i.e., absence of pelvic pathology) which usually starts within 6–12 months after menarche, once the ovulatory cycles are established. Pain symptoms starting beyond 1 year after menarche should raise the suspicion of secondary dysmenorrhea, of which endometriosis may be the underlying pathology. Primary dysmenorrhea usually responds well to medical treatment with NSAIDs or the combined oral contraceptive (COC) pill. It

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was reported in 1990s that 69–73% of teenagers who did not respond to this form of treatment had pelvic endometriosis [2,3].

A recent systematic review by Janssen *et al.* [4] looked at the prevalence of endometriosis in adolescents with chronic pelvic pain (CPP) or dysmenorrhea in the published literature. They found 15 articles which reported the prevalence of laparoscopically confirmed endometriosis in 880 young girls who had a history or dysmenorrhea, CPP-resistant medical treatment and CPP not necessarily resistant to treatment. When they compiled the data from these articles, the overall prevalence of visually confirmed endometriosis was 62% (range: 25–100%) in all adolescent girls undergoing laparoscopic investigation for pain, 75% (237/314) in girls with CPP resistant to treatment, 70% (102/146) in girls with dysmenorrhea and 49% (204/420) in girls with CPP that was not necessarily resistant to treatment. These results are consistent with the aforementioned earlier articles and indicate high likelihood of finding endometriosis in this group of girls with the pain symptoms, particularly in those resistant to medical treatment. It is, however, possible that there might be an overestimation of prevalence due to positive selection bias, as the nine out of 15 were retrospective studies. Furthermore, definition of CPP was not given in the published articles and there might have been a significant variation of the threshold for the decision to proceed with laparoscopy. Hence, the teenagers included might have been the ones with most severe symptoms and more likely to have endometriosis.

Risk factors

Obstructive type Mullerian anomalies are known to be associated with increased risk of endometriosis in teenagers. This is due to increased retrograde menstruation. Spontaneous resolution of endometriosis has been reported after obstruction to the menstrual flow has been surgically treated [5]. Similar to adult endometriosis, family history would also be expected to increase endometriosis in young girls as well [6].

A number of studies suggested early menarche and history of early onset dysmenorrhea as risk factors for endometriosis. A systematic review by Nnoaham *et al.* [7] analyzed 18 case–control studies and found that early menarche slightly increased the risk of endometriosis. An Australian case–control study looked at early menstrual cycle characteristics of 268 women who had a diagnosis of moderate and severe endometriosis [8]. They found that menarche at age ≥ 14 years was strongly and inversely associated with endometriosis and a history of dysmenorrhea was associated with subsequent endometriosis.

Clinical characteristics

Stage of disease

Traditionally, teenage endometriosis was reported to be mild. Rees *et al.* [3] reported that only 8.1% (4/49) adolescents in their series had stage III or IV disease and in the series by Laufer *et al.* [2] all of the 39 girls with endometriosis had stage I or II disease, according to the revised American Society of Reproductive Medicine (rASRM) classification. However, later studies showed that much higher proportion of young girls have advanced endometriosis. In our case series published in 2006, 54.5% of young girls with endometriosis had stage IV disease; two of these had rectovaginal disease, two had both rectovaginal and uterovesical disease, one had rectosigmoid disease and one ureteric disease [9]. Similarly, other reports gave significant proportion of advanced disease in teenagers with endometriosis (Davis *et al.* [10] 50%, Vicino *et al.* [11] 68.4% and Yang *et al.* [12] 88.9%).

The systematic review by Janssen *et al.* [4] found that 50% of the teenagers had minimal, 27% mild, 18% moderate and 14% severe endometriosis in eight of the 15 studies included, which gave the stage of the disease and used the rASRM staging system. It appears that all stages of endometriosis, including deep endometriosis (DE) and ovarian endometriomas, are found in teenagers and that the condition is not limited to early forms only.

Symptoms

Endometriosis in teenagers may cause the classical symptoms of dysmenorrhea and chronic pelvic pain. There is some evidence that the teenagers may be more likely to present with noncyclical pain, unlike adult women with endometriosis, who are more likely to complain of cyclical pain, in other words, dysmenorrhea [2]. As explained above, the adolescents who do not respond to medical treatment with NSAIDs and/or the COC pill are more likely to have endometriosis. There may be additional bowel symptoms such as dyschezia, constipation, intestinal cramps, exercise pain and bladder pain. Sexually active teenagers may report dyspareunia [13].

Natural course of endometriosis in teenagers

The natural course of endometriosis in teenagers has been a subject of debate. In adults, reports of spontaneous resolution, particularly of superficial lesions, have been published. In teenagers, some authors reported progress of endometriosis in a few patients who underwent a second look laparoscopy after ablative treatment of endometriosis. For this reason, some authors believe that teenage endometriosis is a progressive disease [5].

A study by Chapron *et al.* [14] found that women with DE were more likely to have a history of absenteeism from school and that they were more likely to start the COC pill before 18 years of age due to severe dysmenorrhea. On the basis of these findings, these authors concluded that DE had its roots in adolescence and that endometriosis which started in teenage years progressed to DE in the long term.

Diagnosis

Presence of symptoms in the history, particularly symptoms resistant to medical therapy, should raise the suspicion. There may not be any examination findings and vaginal examination may be inappropriate in teenagers who have not been sexually active. However, rectal examination may be a suitable alternative in this situation. These examinations may show a retroverted uterus with reduced mobility or tender uterosacral/rectovaginal nodules. Ultrasound examination is highly reliable in detecting ovarian endometriomas, but is not helpful with the diagnosis of superficial endometriosis. Hence a normal ultrasound examination does not rule out endometriosis. Transvaginal or transrectal ultrasound examinations, when possible, may be helpful in identifying deep nodules or adherent ovaries in experienced hands. Laparoscopy still remains the gold standard in diagnosing or ruling out pelvic endometriosis.

Management

Medical treatment

Due to high prevalence of dysmenorrhea in teenagers, it is reasonable to treat young girls with this symptom with the classical approach of NSAIDs and/or COC pill. It has to be remembered, however, both primary dysmenorrhea and endometriosis-associated pain can respond to these therapies and that symptomatic improvement does not rule out endometriosis. It would be important to communicate this message to the teenager and her parents/carers. While this approach is expected to improve the symptoms and avoid a significant number of further unnecessary investigations including laparoscopy, it is also possible that the symptoms of endometriosis may be masked, allowing the condition to progress further. There is a need to start prospective research on this topic to establish its long-term benefits and potential disadvantages.

When the pain symptom is resistant to the COC or NSAIDs treatment, high likelihood of endometriosis needs to be kept in mind. In this situation, establishing the diagnosis of endometriosis with further investigations, including a laparoscopy if necessary, would be sensible before using further medical treatment options such as gonadotrophin-releasing hormone analogues (GnRHa).

Levonorgestrel intrauterine system (LNG-IUS) has successfully been used for the treatment of endometriosis-associated pain in adults. However, there is a lack of data on its use in teenagers. It may be inappropriate to use LNG-IUS as a first-line empirical treatment for presumed endometriosis in younger teenagers, but this may be an acceptable option for older teenagers, particularly for those who have been sexually active. LNG-IUS insertion may particularly be a good idea for teenagers who are undergoing laparoscopic treatment for endometriosis as a long-term maintenance treatment [15].

GnRHa treatment in teenagers is reserved for those with surgically confirmed disease only. There is, however, concern over the use of GnRHa in teenagers who are at the critical stage of achieving the peak bone density [16]. Despite this, some authors suggest that GnRHa can be used for treatment of endometriosis-associated pain in teenagers [17]. Caution should be exercised in selecting patients for this type of treatment and alternative options, including surgery, should be given priority. GnRHa may be acceptable for teenagers after the age of 17 years, after completion of bone formation.

There is a paucity of data on the use of progestins in teenagers. This is probably because that there is concern on the long-term use of progestins on bone mineral density. Data from adults show that women who use depomedroxyprogesterone acetate (DMPA) have lower bone mineral density. For this reason the UK NICE recommended that care should be taken in recommending DPMA as a contraceptive to adolescents but that it may be given if other methods are not suitable or acceptable [18].

Surgery

Increasing number of groups has been reporting their outcomes following surgical treatment of endometriosis in teenagers. The majority of these publications were included in the aforementioned systematic review by Janssen *et al.* [4,17]. These publications included treatment either by ablation or excision of endometriosis and some did not specify how endometriosis was treated. Only a few of these articles gave outcome data after surgery. Our small series with excision of endometriosis showed 80% of the teenagers were either pain free or greatly improved after surgery and 20% had partial improvement [9]. Other reports by Roman [6] and Yeung *et al.* [13] also reported good results with excision of endometriosis.

Tandoi *et al.* [19] reported high recurrence rates following surgery, during a 5-year follow-up they found 56% recurrence rate among 57 young women aged ≤21 years. Only 34% of these recurrences were

confirmed laparoscopically and in the remaining 66%, the diagnosis of recurrence was based on symptoms or ultrasound findings. The method of surgery was not described in this article and all patients who were not trying for a pregnancy were recommended to take the COC pill postoperatively. By contrast, Yeung *et al.* [13] found no visual or histological evidence of recurrence in the eight of 17 teenagers (47%) who underwent repeat laparoscopy within 66 months following laparoscopic treatment of endometriosis. Only a third of their patients had taken postoperative medical treatment and for this reason they questioned the place of postoperative hormonal maintenance treatment.

The majority of publications reported use of postoperative medical maintenance treatment, such as the COC pill or LNG-IUS. Some groups even advocate the use of GnRHa treatment. As discussed above, LNG IUS can be inserted at the end of surgery, eliminating the concern of insertion of IUS in the outpatients in this young age patient group.

There is currently no consensus as to whether surgery should be avoided as much as possible, or surgical treatment should be considered at an early stage and should aim to eliminate endometriosis completely, including DE. While some recommend a conservative approach due to high recurrence rates, the others suggest early intervention before more severe lesions develop [5]. Further research is required to determine which approach would offer a better long-term outcome.

Conclusion

There has been increasing awareness of endometriosis in teenagers, but our understanding of the optimum management methods is still far from clear. The clinicians are taking a more proactive approach in the diagnosis and treatment of endometriosis in this young age group and both medical and surgical treatment options are being utilized. There are, however, a number of unanswered questions and the need for prospective data collection/international collaboration is obvious.

Future perspective

There is an urgent need to study the natural course of endometriosis in teenagers, as this is likely to improve our understanding of development of deep endometriosis. Studies should also aim to determine whether early diagnosis and treatment of teenage endometriosis lead to better long term outcomes or simply increase number of interventions without preventing progression of the disease.

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Executive summary

- Endometriosis is common in teenagers who have chronic pelvic pain or dysmenorrhea which are resistant to medical treatment with combined oral contraceptives or NSAIDs.
- The risk factors include obstructive Mullerian anomalies and early menarche.
- All stages of endometriosis are found in teenagers, including deep endometriosis.
- Adult endometriosis, particularly deep endometriosis, probably has its roots in adolescence and there is a possibility that teenage endometriosis is a progressive disorder.
- Both surgical and medical treatment approaches are used for treatment in this age group, but care should be taken when treatment with GnRHa and progestins is being considered due to their potential impact on bone formation.

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