

Adolescent Endometriosis

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Abstract

Endometriosis is a common finding in adolescents who have a history of chronic pelvic pain or dysmenorrhoea resistant to medical treatment, however the exact prevalence is unknown. Both early/superficial and advanced forms of endometriosis are found in adolescents, including ovarian endometriomas and deep endometriotic lesions. Whilst spontaneous resolution is possible, recent reports suggest that adolescent endometriosis can be a progressive condition, at least in a significant proportion of cases. It is also claimed that deep endometriosis has its roots in adolescence. Optimum treatment is far from clear and long term recurrence is still a significant problem. The most frequently reported treatment approach in the published literature is a combination of surgery and postoperative hormonal treatment with the combined oral contraceptives, progestins, levonorgestrel intrauterine system or gonadotrophin releasing hormone analogues. Use of gonadotrophin releasing hormone analogues and long term progestins should be carefully considered due to concerns over continuing bone formation in this age group. There is currently no consensus as to whether surgery should be avoided as much as possible to prevent multiple operations in the long term, or surgical treatment should be considered at an early stage before more severe lesions develop. Further research is required to determine which approach would offer a better long term outcome.

Endometriosis is frequently described as an enigmatic condition due to many unanswered questions and controversies in its pathogenesis, diagnosis and management. Endometriosis in adolescents is no exception and is certainly a common subject for debate in the relevant circles. These controversies relate to, but not limited to, its prevalence, natural course and treatment, and can be summarised as follows:

1. Is endometriosis rare in adolescents, as suggested by epidemiological studies which show less than 2% of patients who have a diagnosis of endometriosis are adolescents?
2. Is endometriosis in adolescents more likely to resolve spontaneously, or a progressive condition which eventually leads to severe or deep endometriosis?
3. Is the well publicised concept of delayed diagnosis in adolescence responsible for the finding of severe disease in later life?
4. Are only early forms of endometriosis found in adolescents?
5. Is it better to avoid surgery in adolescents and try empirical and/or medical treatment in preference to surgery?
6. Is empirical treatment harmful in the long term by masking the symptoms and delaying diagnosis, or is it beneficial by avoiding surgery and its associated morbidity?

The majority of these questions remain unanswered, or the responses may be opinion-based instead of evidence-based. Furthermore, many clinicians are less familiar with dealing with patients in this age group. As endometriosis is a potentially chronic condition, adolescents with endometriosis may endure the consequences of this disease for much longer, compared to adult women.⁽¹⁾ As a result, management of adolescent endometriosis poses a significant challenge to the patients and clinicians alike.

Epidemiology

The exact prevalence of endometriosis in adult female population is unknown and the reported figures are based on estimates. The prevalence is thought to be 4% (range 1.5-50%) in fertile women undergoing sterilisation and 13.5% (range 2-68%) in

infertile women.(2) The reported prevalence in women undergoing laparoscopy for chronic pelvic pain varies between 15 to 75%.(3) The wide variation is likely to originate from differences in the level of threshold for diagnostic laparoscopy and/or visual detection rates of endometriotic lesions.

The prevalence in adolescent population is even less clear and the estimates are based on smaller numbers. A systematic review by Janssen et al(4) looked at 15 articles published between January 1980 and December 2011, which reported the prevalence of laparoscopically confirmed endometriosis in 880 young girls with chronic pelvic pain (CPP) or dysmenorrhoea in the published literature. They calculated that the overall prevalence of visually confirmed endometriosis was 62% (range 25–100%) in all adolescent girls undergoing laparoscopic investigation for pain. The prevalence was 75% (237/314) in girls with CPP resistant to treatment, 70% (102/146) in girls with dysmenorrhoea and 49% (204/420) in girls with CPP that was not necessarily resistant to treatment.

These results are consistent with earlier articles which reported that 69-73% of teenagers who did not respond to medical treatment had pelvic endometriosis (5;6) and indicate high likelihood of finding endometriosis in this group of girls with pelvic pain symptoms, particularly in those resistant to medical treatment. It has to be remembered that dysmenorrhoea is a common symptom in teenagers and that it affects up to 40-50% of young women, with severe forms in 15%.(7) It is also quite likely that there might be an overestimation of prevalence of adolescent endometriosis due to positive selection bias, as the nine out of 15 articles included in the review by Jansen et al(4) 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. A recent report from Germany showed that 0.05%, 1.93% and 6.1% of patients were in 10-14, 15-19 and 20-24 year age groups respectively (Haas et al 2013).(8) These numbers suggest that endometriosis is less likely to be diagnosed in girls under the age of 20 years, compared to older women. This may be due to clinicians and/or patients, or their families having a higher threshold in agreeing to and carrying out a laparoscopy in the younger age group.

Reported risk factors for adolescent endometriosis include early menarche, positive family history and obstructive type Mullerian anomalies. An Australian case control study looked at early menstrual cycle characteristics of 268 women who had a diagnosis of moderate and severe endometriosis.(9) They found that women who had their menarche at age 14 years or later were less likely to develop endometriosis. Similarly, a meta analysis by Nnoaham et al(10) which analysed 18 case control studies found that early menarche slightly increased the risk of endometriosis.

A positive family history may be found more frequently in adolescents with endometriosis, a number of case series reporting a first degree relative with endometriosis in 25-30% of the patients.(11;12)

Mullerian anomalies with obstruction may increase the risk of endometriosis from an early age due to increased retrograde menstruation. Fifteen of the 63 (23.8%) adolescents in a case series from China had a Mullerian anomaly, mostly an obstructive type.(13) Spontaneous resolution of endometriosis has been reported after obstruction to the menstrual flow has been surgically treated (14).

Clinical features and natural history

Adolescents with endometriosis tend to present with pain symptoms, as infertility in this age group is unlikely, although it has been reported. In a recent report from France, five of 55 (9%) girls aged between 12 and 19 years had a history of infertility.(11) The most common type of pain in adolescents with endometriosis is the classical dysmenorrhoea and chronic pelvic pain.(11;13) Adolescents may be more likely to present with non-cyclical pain, unlike adult women with endometriosis, who are more likely to complain of cyclical pain, i.e dysmenorrhoea.(5) Other symptoms include dyschezia, constipation, intestinal cramps, exercise pain and bladder pain. Sexually active teenagers may report dyspareunia (15).

Earlier reports suggested that endometriosis in adolescents were exclusively or mostly early stage (revised American Society of Reproductive Medicine Stage, rASRM Classification Stage I and II). Rees et al(6) 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(5) all of the 39 girls with endometriosis had stage I or II disease. 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 fifteen studies included, which gave the stage of disease and used the rASRM staging system. 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.(16) Similarly, other reports gave significant proportion of advanced disease in teenagers with endometriosis (Davis et al(17) 50%, Vicino et al(18) 68.4% and Yang et al(13) 88.9%). The recent report from France showed 40% of 55 adolescents had stage III or IV disease, including 6 girls with deep endometriosis (DE).(11)

It appears that all stages of endometriosis, including DE and ovarian endometriomas, are found in teenagers and that the condition is not limited to early forms only.

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. Spontaneous regression may be as high as 42% as demonstrated in prospective randomised controlled trials which included repeat laparoscopies with an at least six months interval and progress is seen only in 29% of patients.(19) In adolescents, 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.(14) The recent French case series(11) reports rather interesting follow up data from 50 adolescents on progress; in addition to the initial diagnosis of six DE cases, nine more patients were found to have developed DE at repeat laparoscopy. Furthermore, three (50%) of the original six patients later developed recurrent DE, giving a total of 12 cases with DE during follow up. The same report also showed five new cases and seven recurrent (35.84%) endometriomas during the follow up period.

A study by Chapron et al(20) 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 dysmenorrhoea. 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 and Management

Presence of symptoms in the history, particularly pain resistant to medical therapy, should raise the suspicion of endometriosis in adolescents. There may not be any examination findings and vaginal examination may be inappropriate in teenagers who have not been sexually active. Examination 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. A pelvic mass was detected in 87% (55/63) in the report from China(13) and 41.8% (23/55) in the French series(11). Transvaginal or transrectal ultrasound examinations, when possible, may be helpful in identifying deep nodules or adherent ovaries in experienced hands. A normal ultrasound examination in the absence of endometriomas or obvious deep nodules does not rule out endometriosis. Laparoscopy still remains the gold standard in diagnosing or ruling out pelvic endometriosis.(21)

Dysmenorrhoea in adolescence is common and treating young girls with dysmenorrhoea with NSAIDs and/or COC pill is a common practice. Both primary dysmenorrhoea and secondary dysmenorrhoea due to endometriosis can respond to these therapies and symptomatic improvement does not rule out endometriosis. This approach may improve the symptoms and avoid a significant number of further unnecessary investigations including laparoscopy. However, it is also possible that endometriosis may progress whilst the symptoms are masked. Hence, there is an urgent need to start prospective research to establish long term benefits and potential disadvantages of empirical treatment with the COC or NSAIDs.

If the pain symptom persists despite the COC and/or NSAIDs, probability of endometriosis needs to be remembered. In our practice, we aim to establish the diagnosis of endometriosis at laparoscopy, instead of using further medical treatment

options such as gonadotrophin releasing hormone analogues (GnRHa) in this age group.

GnRHa treatment in adolescents is usually reserved for those with surgically confirmed disease. Their side effect profile makes it a relatively difficult choice, and in any case, the treatment would be for a relatively short period due to irreversible bone density loss with long term use. There is also concern over the use of GnRHa in teenagers who are at the critical stage of achieving the peak bone density.(22) However, some authors suggest that GnRHa can be used for treatment of endometriosis associated pain in teenagers.(23) Caution should be exercised in selecting patients for this type of treatment and alternative options, including surgery, should be given priority. GnRHa may be more acceptable for teenagers after completion of bone formation, usually after the age 17 years,

There is a lack of data on the use of progestins in adolescents. This may be again due to concerns over 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 United Kingdom National Institute for Health and Clinical Excellence (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.(24)

Similarly, there is a lack of data on the use of levonorgestrel intrauterine system (LNG-IUS) in adolescents. 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.(25)

Most published reports on the subject of adolescent endometriosis include case series diagnosed and treated surgically. This may be because the published reports are expected to include surgically confirmed cases. The majority of reports suggest postoperative medical/hormonal treatment to address the issue of recurrence.

Publications before 2012 were included in the review by Janssen et al.(4) These publications included treatment either by destruction or removal 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 (16). Other reports by Roman(12) and Yeung et al(15) also reported good results with excision of endometriosis. A recent report by Dun et al(26) which included 25 rASRM stage I – III cases showed resolution or improvement of the pain in 80% of cases one year after surgery, 76% of the patients had been given postoperative hormonal therapy in the form of the COCs or progestins.

Recurrence of symptoms and/or endometriosis is a major concern after surgery in adolescents. This is because recurrence may lead to multiple operations and symptomatic suffering over many years of reproductive age before menopause. In addition, subfertility will be a concern in these patients with a history of endometriosis, particularly in the presence of recurrent symptoms or disease. Recurrence rates following surgery were high in the report by Tandoi et al(27); there was 56% recurrence during a 5 year follow up amongst 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. All patients who were not trying for a pregnancy were recommended to take the COC pill postoperatively. In contrast, Yeung et al(15) 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 recent report by Audebert et al(11), during a mean follow up period of 97.5 months amongst 50 adolescents, only 13 (23%) reported complete or significant resolution of their pain symptoms. Seventeen (34%) patients underwent a second laparoscopy for recurrent pain, there were five new and seven recurrent endometriomas, and nine new and three recurrent DE lesions were detected. Patients were advised to use progestogens, COC or LNG-IUS postoperatively, the number of users and duration of use were unclear in the report.

Data from the published reports with follow up confirm that recurrence of pain and/or disease is a significant problem and it appears to occur regardless of postoperative adjuvant treatment. This picture is probably not dissimilar to the situation in adult women and highlights the long term nature of endometriosis. 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. Whilst some recommend a conservative approach due to high recurrence rates, the others suggest early intervention before more severe lesions develop. Further research is required to determine which approach would offer a better long term outcome.

Conclusions

Adolescent endometriosis appears to be more common than once it was thought to be, although its exact prevalence remains unknown. All forms of endometriosis including endometriomas and DE are present in adolescents and there is evidence that the condition progresses even after treatment, at least in some patients. The diagnosis is often delayed, leading to suffering for several years and, for this reason, there is a need to early diagnosis of endometriosis in adolescents with dysmenorrhoea and CPP. The most frequently reported treatment approach is a combination of surgery and postoperative hormonal treatment, but long term recurrence remains a significant problem. There are a number of unanswered questions and there is a need for research to identify novel treatment approaches which will be more effective in the long term.

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