Review

Noninvasive Diagnosis of Endometriosis in Adolescents and Young Female Adults: A Systematic Review

Inês Jerónimo Oliveira, MD[1,*], Pedro Viana Pinto, MD[2,3,4], João Bernardes, PhD[3,4,5]

[1] *Mestrado Integrado em Medicina, Faculdade de Medicina da Universidade do Porto, Porto, Portugal*
[2] *Serviço de Anatomia, Faculdade de Medicina da Universidade do Porto, Porto, Portugal*
[3] *Departamento de Obstetrícia e Ginecologia, Faculdade de Medicina da Universidade do Porto, Porto, Portugal*
[4] *Serviço de Ginecologia, Centro Hospitalar e Universitário de São João, Porto, Portugal*
[5] *Centro de Investigação em Tecnologias e Serviços de Saúde (CINTESIS@RISE), Faculdade de Medicina da Universidade do Porto, Porto, Portugal*

ABSTRACT

Study Objectives: Our aim was to review the evidence concerning the noninvasive diagnosis of endometriosis in adolescents.
Methods: A systematic review was written following the SWiM reporting guidelines. The study research was made across three databases (MEDLINE/PubMed, Scopus, and Web of Science) to identify articles about the adolescent population and the diagnosis of endometriosis through noninvasive methods. The search included the keywords "endometriosis," "adolescents," "diagnosis," "ultrasound," and "MRI." Only English-language articles were considered, and those published prior to 2000 were excluded. The established outcomes focused on clinical symptoms, ultrasound (US), and magnetic resonance imaging (MRI) findings suggestive of endometriosis.
Results: We included 26 articles, mostly comprising case series and cross-sectional studies. The pooled analysis involved 2,299 female adolescents (age range 8-25 years old) with clinically suspected, imaged, and/or surgically confirmed endometriosis. The most frequently reported symptom was dysmenorrhea, followed by chronic pelvic pain. Among adolescents clinically suspected of endometriosis undergoing ultrasound (US), 32.8% exhibited at least one sign of endometriosis. Of the 167 patients with ultrasound-diagnosed endometriosis, 48.5% had deep infiltrating endometriosis (DIE), and 45.5% had an endometrioma detected. Three studies assessed MRI findings, revealing that 49.8% presented with signs of endometriosis.
Conclusions: Dysmenorrhea and chronic pelvic pain stand out as key symptoms of adolescent endometriosis. Although their diagnostic accuracy varies, US and MRI have emerged as valuable tools for diagnosing the disease. While the US may have limitations, especially in detecting subtle lesions, MRI shows promise, even in cases with normal previous ultrasounds. Early recognition and proactive diagnosis are crucial for improving the management of endometriosis in adolescents.
Key Words: Endometriosis, Adolescent, Diagnosis, Ultrasound, US, Magnetic resonance imaging, MRI

Introduction

Endometriosis is a common gynecological disorder thought to affect around 64% of adolescents with pelvic pain undergoing gynecological investigation.[1] It was first described in adolescents as early as the 1940s.[2] Although more than 4 million women and people assigned female at birth have been diagnosed with the disease, population-based studies show that an estimated 6 of 10 cases are undiagnosed.[3]

This chronic inflammatory disease is defined by endometrium-like tissue outside the uterus, most commonly on the ovary, peritoneum, and adjacent organs like the bladder or rectum.[4] Even though a benign disease, ectopic endometrial tissue may implant and develop an inflammatory reaction responsive to estrogens, leading to dysmenorrhea, dyspareunia, chronic pain, and infertility.[5] Although several theories have been developed over the years, the exact cause behind this disease remains unknown.[6] The natural course of the disease is unclear, and questions persist about the potential progression of superficial endometriosis to other subtypes, spontaneous regression, or implications for infertility, especially in the absence of treatment. The American Society for Reproductive Medicine (ASRM) categorizes endometriosis into four stages (minimal, mild, moderate, and severe), determined by the location, depth, and site of lesions and adhesions.[7] Despite being the most widely used system, multiple revisions of the ASRM classification have not notably enhanced its predictive accuracy for pain, dyspareunia, or infertility.[8,9]

Endometriosis is remarkably responsible for a decrease in women's quality of life (QOL), not only due to the physical discomfort it causes but also because of the mental and emotional burden involved,[10] both in adults and adolescents. It has been shown that dysmenorrhea occurs in 16% to possibly as high as 93% of adolescent girls and is the leading cause of recurrent short-term school absence in this age group.[11] A survey analysis demonstrated that women with endometriosis often begin to report symptoms in their adolescence, with 70% of the patients reporting before age 20 and nearly 40% before 15 years old.[12]

Diagnosis of endometriosis remains a challenge worldwide, especially for women who first experience symp-

The study has taken place at Porto, Portugal—University of Porto.

* *Address correspondence to*: Inês Tomás Jerónimo Oliveira, Faculty of Medicine, University of Porto, Alameda Professor Hernâni Monteiro, 4200-319, Porto, Portugal
E-mail address: inesjeronimo.oliveira@gmail.com (Inês Jerónimo Oliveira).

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toms at a young age. Recent evidence points out that it takes around 8 years to diagnose this disorder[13] and the median delay in diagnosis increases if the symptoms are present in adolescence.[13,14] The lack of pathognomonic features or biomarkers,[15] the absence of an accurate and sufficient noninvasive diagnostic test,[16,17] and the variability in symptom patterns over time[18] illustrate the difficulty imposed on clinicians, especially general practitioners, in the diagnosis of this disease. Furthermore, the disease in its earlier stages may be associated with different imaging and laparoscopic signals. To worsen the scenario, it is also known that the awareness of endometriosis in adolescents among medical professionals is low.[19]

Since symptoms of endometriosis usually begin in adolescence[20] and the huge future medical and social consequences associated, an approach in this age group becomes even more important. Furthermore, it is recognized that early lesions, although smaller and subtler, may be associated with more severe symptoms than bigger and more fibrotic lesions, that are less metabolically active and inflammatory.[6] Treating the disease before central sensitization occurs may be key to guaranteeing a better quality of life for these patients. Furthermore, the need for a laparoscopy to make a diagnosis of this disease is, nowadays, not adequate for adult women and maybe even less for adolescents.

In the present study, our aim was to review the evidence concerning the noninvasive diagnosis of endometriosis in adolescent patients. This contribution seeks to enhance our understanding of the appropriate approach for this specific population.

Methods

This systematic review was conducted according to PRISMA 2020 guidelines. The systematic review protocol is registered in the international PROSPERO database as No. CRD42023457516. Considering that this study was a systematic review, an Institutional Review Board was not required. Efforts were made to use gender-neutral language; however, gendered language appears in some instances due to references to historical research articles.

Search Strategy

We aimed to assess how endometriosis is diagnosed in adolescent-assigned female at birth and, more specifically, which noninvasive diagnostic procedures are being applied to adolescents with suspected endometriosis to achieve an early diagnosis. We took into consideration a variety of studies from 2000 onward in this analysis. Randomized controlled trials (RCTs), prospective cohort studies, case-control studies, retrospective cohort studies, and case series were screened.

We searched three databases: MEDLINE/Pubmed, Scopus, and Web of Science. The search strategy used was the query ("adolescent" OR “adolescence” OR “adolescents” OR “pediatric” AND “endometriosis” AND [“diagnosis” OR “ultrasound” OR “MRI”]), on August 24, 2023. The search was limited to publications in the English language and articles published earlier than 2000 were excluded. The reference list of the included studies and relevant reviews on the matter were analyzed to identify other studies for potential inclusion in this article.

Inclusion and Exclusion Criteria and Study Selection

All records identified using our search strategy were independently screened by two authors based on the titles and abstracts, applying predetermined inclusion and exclusion criteria. Any discrepancies were resolved by consensus, and different interpretations were resolved by a third author. The second selection stage was based on reviewing the full text of potentially relevant articles. The same independent reviewers read relevant full-text articles for inclusion.

Articles were included if the following inclusion criteria were met: (1) adolescent population defined as patients between 10 and 24 years old, as defined by Sawyer et al.[21] or patients that were referred to as “adolescent” or “teenager”; (2) adolescents assigned female at birth who either have clinically suspected endometriosis or have received a diagnosis of endometriosis; (3) the outcome refers to the diagnosis of endometriosis using noninvasive methods (clinical symptoms and/or imaging) or where the invasive diagnosis is compared with the noninvasive methods; and (4) observational studies or interventional studies.

We excluded nonoriginal studies classified as guidelines, reviews, conference abstracts, editorials, opinion articles, or protocols, as well as case reports and articles where the full-text manuscript was not available, after efforts to contact authors.

Articles that did not perform an age-based cluster analysis—which would have made it impossible to extract data, especially for the intended adolescent population—or those only concentrated on adult women who were 18 years of age or older were omitted.

EndNote was utilized to exclude duplicated studies during the study selection process, while Rayyan software was accessed to assist in organizing and selecting eligible studies.

Quality Assessment

Quality assessment of cohort and cross-sectional studies was conducted using the Newcastle-Ottawa Scale (NOS).[22] For the cross-sectional studies, an adapted NOS was used[23] and to evaluate the methodological quality of the case series and address potential biases in their conduct, we used the JBI (Joanna Briggs Institute) Critical Appraisal tool.[24]

Data Extraction

The following data was independently extracted from each of the studies into a spreadsheet: authors, publication year, country, study design, study period, studied population, number of participants either with clinically suspected and/or with the confirmed diagnosis of endometriosis by imaging and/or laparoscopically. Other items in-

cluded were the noninvasive diagnosis imaging modality mentioned/used, outcomes of interest, and the aim of the study. Study outcomes on the clinical presentation of endometriosis, ultrasound (US), and magnetic resonance imaging (MRI) findings of endometriosis, and rASRM classification data from patients that have undergone laparoscopy or laparotomy were extracted too. A standardized table was created for each outcome after the data from the included studies was extracted. The studies were categorized based on the outcomes that were classified by the nondiagnostic tools used, such as clinical diagnosis, US findings, and MRI findings. This was thought to be the most transparent method of reporting the results.

All studies results were combined, and since this condition significantly affects quality of life and none of the studies indicated a high risk of bias, none of the results were chosen for prioritization.

Results

Our search identified a total of 1197 articles, and 281 duplicates were excluded. After a review of 916 titles and abstracts, we retained 84 full-text articles for eligibility. Among them, 26 articles were included: two cohort, one case-control, four cross-sectional, and nineteen case-series studies. A flow diagram was created using a PRISMA flowchart to describe this search method (Fig. 1) and the main study characteristics are displayed in Table 1.

Overall, the analysis included a total of 2, 167 female adolescents with a clinical and/or imagological suspected diagnosis of endometriosis. From the population included, 1,124 (51.9%) female adolescents underwent laparoscopy for a definitive diagnosis of endometriosis. The term “adolescents" was defined differently in each study, with some authors sticking to the World Health Organization definition (up to 19 years old), while others defined it until 25 years old. The age range of the population studied was from 8 to 25 years old, and the weighted mean of ages was 18.2 years old, calculated with the findings presented in 21 articles; five articles were excluded for this calculation due to a lack of reports of individual patient ages. This systematic review covered cases from several continents.

Among the 19 case series studies assessed using the JBI Critical Appraisal Checklist, 16 were deemed to have a “low" risk of bias, while three were categorized as having a “moderate" risk. Cross-sectional studies, evaluated through the NOS, scored between 5 and 7 points out of 10, with notable weaknesses in the selection process. The case-control study, with a NOS score of five out of nine points, demonstrated bias in the representativeness of cases, selection of controls, and comparability. Cohort studies, despite the highest risk of selection bias, were considered to be of high quality. Bias assessment and evaluation are demonstrated in Supplementary Table S1.

Clinical Characteristics of Endometriosis in Adolescents

The clinical symptoms and physical examination findings of endometriosis in adolescent patients were assessed in 23 articles (Table 2).

The typically reported symptoms of endometriosis, such as dysmenorrhea and chronic pelvic pain, were encompassed by less typical symptoms, such as vague abdominal pain and gastrointestinal and genitourinary symptoms. Of the total of 1426 endometriosis patients included in this analysis, dysmenorrhea was the predominant symptom, reported by 82.9% of adolescent girls (1182 patients). Furthermore, 43% reported having chronic, acute, or acyclic pelvic discomfort, 18% abnormal uterine bleeding, and 19% gastrointestinal symptoms. Dyspareunia was reported by 13.7%, and urinary complaints were scarcely reported (6.6% of patients). Infertility was also a rare complaint (2.1%) since a great proportion of adolescents were not sexually active.

Khashchenko et al.[25] revealed moderate-severe dysmenorrhea in 97.8% (95.6% persistent to NSAIDs) of adolescents with laparoscopically confirmed peritoneal endometriosis (PE). High-intensity pain (7.5 ± 2.1 vs 2.5 ± 2.3 in the control group, VAS points, $P < .001$) that most often began one day before menses and lasted three days into menses was reported; the majority (63.3%, 57/90) reported the symptoms since menarche, and approximately 15.6% experienced pain daily. DiVasta et al.[18] reported endometriosis symptoms starting at 13 years old on average; Martire et al.[26] found more painful symptoms in adolescents with US signs of endometriosis.

Al-Jefout's study[27] found a significant association ($P = .039$) between endometriosis and cold intolerance, particularly in those with generalized anxiety disorder.

The majority of cases described (74.2%) had mild to moderate disease according to the ASRM (Supplementary Table S2), with studies, such as Marsh et al.[28] and Unger et al.[29] with no cases of severe endometriosis (stages III and IV).

US Findings

Overall, only eight studies reported US findings in patients with endometriosis (Table 3).

Among the 729 adolescents who underwent US testing and were clinically suspected of having endometriosis, 30.6% exhibited at least one ultrasound marker indicative of the disease. Out of the 167 patients with ultrasound-confirmed endometriosis (transvaginal/transrectal), 45.5% presented with endometrioma, 48.5% had deep infiltrative endometriosis (DIE), 40.1% showed signs of adenomyosis, and 13.7% displayed adhesions.

Martire et al.[26] included in their study adolescents with transvaginal/transrectal ultrasound for different clinical indications. From this population, 36 adolescents had at least one sign of endometriosis; DIE was detected in ten adolescents. The symptom that exhibited the strongest correlation with ultrasound findings of endometriosis was dysmenorrhea, reported in 86.1% of the patients. In their study in 2023,[16] there was a statistically significant difference in the number of cases between early adolescents (12-16 years—27/39 with normal ultrasound) and young women (21-25 years—90/211 with normal ultrasound); the majority of patients with US signs had posterior DIE (53.4%, the majority

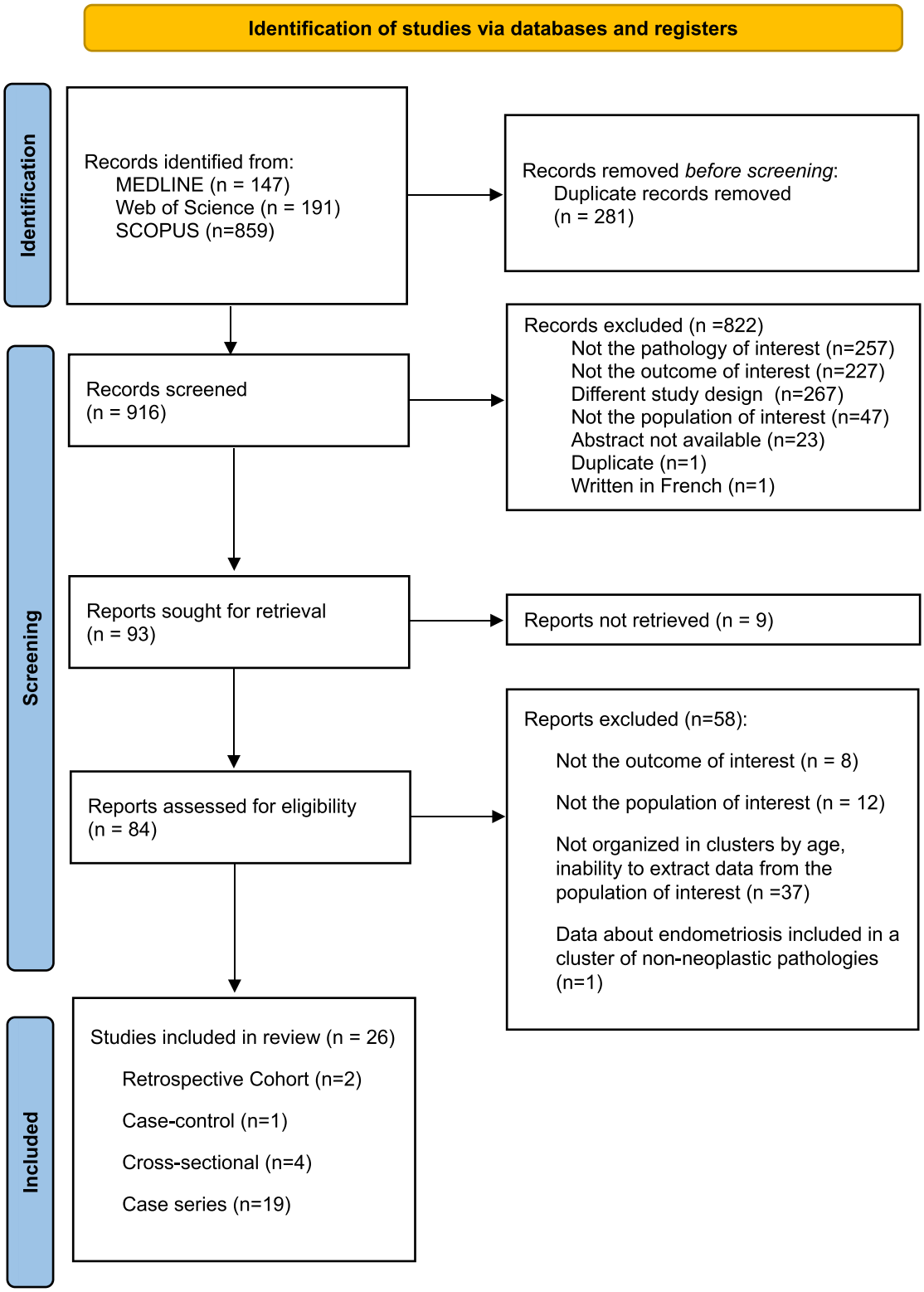

Fig. 1. PRISMA flowchart showcasing the search method.

in the uterosacral ligaments) and an endometrioma (41.2%). Only one case of anterior DIE was identified in both studies.

In the articles with a laparoscopic diagnosis of endometriosis, two only described a pelvic mass in the US, which is neither specific or adequate for diagnosis of the disease.[30,31] In the study by Yang et al.[30] adolescents with genital tract malformations had mainly ovarian endometriosis (14/15), while adolescents with a normal genital tract had both, DIE (26/48) and ovarian endometriosis (41/48).

Even though no generally accepted endometriosis markers were described by Khaschenko et al.[25] the authors

Table 1
Characteristics of Included Studies in our Systematic Review.

Author, Year	*Country*	*Study Design*	*Study Period*	*Population of the Study**	*N. Par.*	*Mean Age*	*NID Image*	*Outcomes of Interest*	*Aim of the Study*
Bai et al. (2002)[58]	Korea	Retrospective analysis; case series	1990-1999	Adolescent girls aged 14 to 21 years old, who had undergone a laparotomy or laparoscopy and were diagnosed with endometriosis.	39	20.1	-	Chief symptoms leading to the diagnosis, clinical stage, age distribution, and treatment modality.	Evaluate the age distribution, diagnosis, clinical stage, and treatment for endometriosis in adolescents in Korea.
Marsh et al. (2005)[28]	USA	Case-series	-	Premenarcheal girls, aged 8 to 13 years old, with chronic pelvic pain of unclear origin who underwent US and laparoscopic excision of endometriotic lesions.	5	-	US	Visual presence of endometriosis and decrease in pelvic pain after destruction of lesions.	Identify endometriosis as a cause of chronic pelvic pain in premenarcheal girls without an obstructive anomaly of the reproductive tract.
Roman et al. (2010)[59]	New Zealand	Comparative cohort	2003-2009	Female patients aged 14 to 19 years old, who underwent operative laparoscopy at Braemar Hospital with the presumptive diagnosis of endometriosis.	20	17.4	US; MRI	Chief complaint at the initial consultation; gynecological examination findings; VAS for endometriosis-related symptoms; surgical findings.	Describe their experience with laparoscopic excision of endometriosis in an adolescent population and compare it with a nonadolescent population treated during the same period.
Vicino et al. (2010)[43]	Italy	Prospective analysis; case-series	2005-2006	Females aged ≤21 years who had a first surgically confirmed diagnosis of endometriosis.	38	18.6	-	Age at diagnosis, symptoms at presentation, and stage of disease according to rASRM classification.	Analyze the clinical manifestations of endometriosis in adolescents.
Tandoil et al. (2011)[44]	Italy	Retrospective analysis; case series	2000 - 2005	Female aged 16 to 21 years old with a surgically and histologically confirmed first diagnosis of endometriosis by laparoscopy or laparotomy.	57	19	US	Recurrence of endometriosis after conservative surgery for endometriosis based on clinical symptoms, physical examination, and US findings.	Determine a profile of women with a consistently higher risk of recurrence who may benefit from specific management strategies.
Unger et al. (2011)[29]	USA	case-series	-	Patients aged 13 to 16 years old, with complaints of severe pelvic pain, and diagnosed with stage 1 endometriosis at the time of laparoscopy.	3	14	-	Clinical presentation.	Describe 3 cases of endometriosis progression in adolescents who did not maintain medical regimen postoperatively.
Yeung et al. (2011)[60]	USA	Prospective analysis; case series	1999-2007	Teenagers aged 12 to 19 years old, with symptoms suspicious for endometriosis who underwent laparoscopic excision.	17	-	-	Rate of recurrent (or persistent) endometriosis.	Determine long-term outcomes after complete laparoscopic excision in a teenage population.
Yang et al. (2012)[30]	China	Retrospective analysis; case series	1992-2010	Patients aged 12 to 20 years of age who underwent surgery and had a pathologically confirmed diagnosis of endometriosis.	63	18,4	US	Clinical symptoms, preoperative ultrasound findings, surgical procedures, and findings, and postoperation management (recurrence).	Present the experience in diagnosis, management, and follow-up of endometriosis in a Chinese adolescent population.

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Table 1 (*continued*)

Author, Year	*Country*	*Study Design*	*Study Period*	*Population of the Study**	*N. Par.*	*Mean Age*	*NID Image*	*Outcomes of Interest*	*Aim of the Study*
Lee et al. (2013)[45]	Korea	Cross-sectional	2003-2010	Adolescent females ≤ 20 years old who underwent laparoscopic surgery for the treatment of endometrioma.	35	19.2	-	Clinical characteristics include demographic factors, menstrual patterns, and characteristics of endometriosis.	Evaluate the clinical characteristics of endometrioma in adolescent women compared to women of other age groups.
Özyer et al. (2013)[49]	Turkey	Retrospective analysis; case series	2007-2011	Adolescent females and young women, aged 17 to 24 years old who underwent laparoscopic surgery for ovarian endometrioma.	63	22	US	Symptoms on admission; endometriosis characteristics during surgery; Adnexal adhesions according to rASRM classification.	Evaluate clinical aspects of endometriomas encountered in late adolescent females and young women and to review the issues specifically related to the disease in this age group.
Andres et al. (2014)[61]	Brazil	Retrospective analysis; case series	2008-2013	Patients, aged 13 to 20 years old, undergoing surgery with a histological diagnosis of endometriosis.	21	17.9	US; MRI	The clinical condition of adolescents with Endometriosis.	Report the clinical characteristics of adolescent patients with endometriosis.
Smorgick et al. (2014)[47]	USA	Retrospective analysis; case series	2000-2011	Adolescents and young women who underwent surgery for suspected/confirmed endometriosis and were ≤22 years old at the time of surgery.	86	19.9	-	Pain symptoms; indication for surgery; endometriosis stage reported according to the revised AFS classification.	Describe the prevalence and characteristics of advanced-stage endometriosis in adolescents and young women.
Timur et al. (2015)[62]	Turkey	Retrospective analysis; case series	2008-2012	Patients < 18 years who underwent an operation for an adnexal mass.	41	14.5	US; MRI	Complaints during admission, images of the masses that were detected with different modalities, laboratory findings, applied surgical procedures, and pathology findings.	Evaluate preoperative findings, surgical procedures, and histopathologic findings of the adolescent patients who had surgery for adnexal mass.
Dun et al. (2015)[11]	USA	Retrospective analysis; case series	2001-2009	Adolescent females, aged 10 to 21 years old with endometriosis diagnosed during laparoscopy for pelvic pain.	25	17.2	-	Symptoms, time from onset of symptoms to correct diagnosis, number, and type of medical professionals seen, diagnosis, treatment, and postoperative outcomes.	Describe the experience of adolescents who underwent laparoscopy for pelvic pain and were diagnosed with endometriosis.
Ragab et al. (2015)[32]	Egypt	Cross-sectional	2012-2014	Adolescent school girls from 3 different schools covering rural and urban areas in Egypt, with symptoms and signs suggestive of endometriosis.	56	15.2	US; MRI	Symptoms of endometriosis, the accuracy of abdominal US, MRI, and laparoscopic findings.	Determine the prevalence of endometriosis among adolescent school girls with severe dysmenorrhea.
Audebert et al. (2015)[31]	France	Retrospective analysis; case series	1998-2013	Adolescents, aged 12 to 19 years old who underwent surgical treatment for endometriosis.	55	17.8	US; MRI	The main indications for surgery, are preoperatively ultrasound findings, medical history, family history of endometriosis, operative findings, clinical symptoms, and MRI findings at follow-up.	Illustrate the different clinical presentations of these cases while providing accurate follow-up data, with a focus on the recurrence of symptoms, disease, and fertility outcomes.

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Table 1 (*continued*)

Author, Year	*Country*	*Study Design*	*Study Period*	*Population of the Study**	*N. Par.*	*Mean Age*	*NID Image*	*Outcomes of Interest*	*Aim of the Study*
Fong et al. (2017)[46]	Singapore	Retrospective analysis; case series	2000-2007	Patients aged 14 to 25 years old who had laparoscopy for suspected endometriosis, with histological.	45	-	US	Presenting symptoms, Investigation findings (preoperative US).	Describe the disease pattern in a group of young Asian women with a histological diagnosis of endometriosis.
Matalliotakis (2017)[63]	Greece	Retrospective analysis; case series	1996-2016	Patients aged 13 to 21 years old who underwent surgical treatment for endometriosis using laparoscopy or laparotomy.	55	18.3	-	Presenting symptoms, age at menarche, history of asthma, obstetric outcome, family history, and congenital malformations.	Evaluate endometriosis in adolescents and young girls; review the menstrual, reproductive characteristics, and risk factors.
Al-Jefout et al. (2018)[27]	Canada	Prospective analysis, case series	2010-2014	Female patients, aged 15 to 21 years old, who had CPP refractory to conventional medical therapy.	28	18.4	US	Presence and stage of endometriosis at laparoscopy, the presence of cold intolerance, and the severity and duration of pain symptoms.	Explore the prevalence and clinical manifestations of endometriosis in young women with CPP refractory to conventional medical therapy.
DiVasta et al. (2018)[18]	USA	Cross-sectional	2012-2016	Adolescents (diagnosed at ≤18 years old) with surgically confirmed endometriosis.	295	16	-	Clinical presentation-self-reported pain, dysmenorrhea, urinary or bowel movement habit changes, infertility.	Elucidate the symptom presentation of adolescents as compared with adults to determine whether differences existed, based on age at surgical diagnosis that could impact time to diagnosis.
Stochino-Loi et al. (2020)[37]	France, Switzerland, Denmark	Retrospective analysis; case series	2009-2014	Adolescent patients, aged < 20 years old, who underwent surgical management of symptomatic endometriosis.	32	-	-	Main baseline painful symptoms compared between groups of age.	Assess the relationship between age, location of the disease, and surgical procedures performed in patients undergoing surgical management of endometriosis.
Martire et al. (2020)[26]	Italy	Retrospective analysis; case series	2014-2019	Adolescent patients aged 12 to 20 years, who received a pelvic US examination with a transvaginal (TVS) or transrectal (TRS) probe.	205	18	US	Locations of endometriosis were recorded using a dedicated ultrasound mapping sheet and the severity of painful symptoms.	Evaluate the ultrasonographic presence of different forms of endometriosis and the associated clinical symptoms in adolescent women.
Khashchenko et al. (2023)[25]	Russia	Case-control study	2020-2022	Cases: Girls from menarche to 17 years old with a laparoscopically confirmed diagnosis of peritoneal endometriosis (PE); Controls: healthy adolescent girls of the same age with regular periods and no gynecological and endocrine pathologies.	90 (cases)	16	US; MRI	Clinical symptoms, diagnostic accuracy of VAS score; US for the pelvic organs; MRI—frequency of suspected PE, location of endometriotic foci, and accuracy of signs in the prediction of laparoscopic confirmation of PE.	Compare the clinical features, instrumental diagnostics, and surgical and histological peculiarities in adolescent patients with peritoneal endometriosis.

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Table 1 (*continued*)

Author, Year	*Country*	*Study Design*	*Study Period*	*Population of the Study**	*N. Par.*	*Mean Age*	*NID Image*	*Outcomes of Interest*	*Aim of the Study*
Martire et al. (2023)[16]	Italy	Retrospective analysis; case series	2016-2021	Women aged 12–25 years were referred to a gynaecological ultrasound (US) Unit with severe dysmenorrhea.	304	20.8	US	Locations of endometriosis using the US; Painful symptoms correlated to the different endometriosis forms.	Diagnose endometriosis in young patients ≤ 25 with severe dysmenorrhea through US findings and correlate the symptoms to its different forms.
Millischer et al. (2023)[33]	France	Prospective analysis; cross-sectional	2019-2020	Adolescents aged 12-20 years who underwent MRI for severe dysmenorrhea.	345	17.4	MRI	Data on the endometriosis phenotypes (OMA and/or DIE) and distribution of anatomical lesions; The severity of painful symptoms.	Evaluate the prevalence of MRI of ovarian endometrioma (OMA) and deep infiltrating endometriosis (DIE) in adolescents presenting with severe dysmenorrhea.
Wüest (2023)[34]	Switzerland	Retrospective cohort study	2017-2020	Patients, aged 15 to 24 years old, with a diagnosis of endometriosis (either clinically suspected, diagnosed by examination and imaging, or confirmed by surgery).	144	-	US; MRI	The difference in the severity of the symptoms between 2 age groups, with and without hormonal treatment.	Analyze the clinical characteristics and severity of symptoms in adolescent patients with endometriosis compared with older patients.
Total					2167	18.2*			

N. Par: number of participants with clinically and/or imagistically suspected and/or confirmed diagnosis of endometriosis; NID: noninvasive diagnosis method used; US: ultrasound imaging; MRI: magnetic resonance imaging; rASRM: revised American Society of Reproductive Medicine classification; CPP: chronic pelvic pain.

* Weighted mean.

found a significant correlation between uterine wall thickness and peritoneal endometriosis in 3.3% of the adolescent population under study.

Pelvic MRI Findings

Table 4 represents the three studies that included the MRI findings of adolescent patients with suspected or confirmed endometriosis.

Among 22 patients in the study by Ragab et al.[32] with severe dysmenorrhea and positive ultrasound for endometriosis who declined laparoscopy, an MRI had findings consistent with endometriosis in 77.3% ($n = 17$).

Of the 308 adolescent girls included in Millischer et al.[33] 39.3% presented with endometriosis signs at MRI, the majority (88.9%) with DIE; 11.4% had also signs of adenomyosis. The majority of ovarian endometriomas occurred in those aged ≥ 18 years, while retrocervical lesions were observed from a young age (<15 years). Rectosigmoid lesions were rare (3.3%), with all the intestinal lesions diagnosed after the age of 17 years. Ureteral or bladder involvement was absent. Interestingly, 107 adolescents with endometriosis suspected in the MRI had a previous ultrasound without suspicion of the disease.

In the Khashchenko et al.[25] study, 78.9% of pediatric patients showed MRI signs of PE, mainly in the uterosacral ligaments (39.4%), parametrium (38.0%), pouch of Douglas (25.4%), and peritoneum of the ovarian fossae (29.6%).

Discussion

Despite being widely researched in adult women, endometriosis presents a variety of difficulties for clinicians, particularly when it comes to adolescents. Given the limited literature surrounding diagnostic characteristics in this population, the management approach often relies on extrapolated data gathered from adults. This study collected data to enhance our understanding of this disease in adolescents and the efficacy of the noninvasive tools at our disposal to achieve an early diagnosis, showing that dysmenorrhea and chronic pelvic pain are the most common symptoms of the disease in adolescents and that ultrasound and MRI may have an important role in its diagnosis. All the subtypes of endometriosis were diagnosed, going through peritoneal lesions, ovarian endometriosis, and DIE.

Clinical Characteristics of Endometriosis in Adolescents

Overall, adolescents with endometriosis commonly experience severe dysmenorrhea resistant to conventional treatments such as contraceptive pills, NSAIDs, or antispasmodics. The second most frequently reported symptom was pelvic pain, which, when coupled with persistent dysmenorrhea despite pharmacological treatments, strongly correlates with the presence of endometriosis. Nongynecologic symptoms may also occur frequently in adolescents

Table 2
Studies Evaluating the Clinical Symptoms and Physical examination Findings of Endometriosis in Adolescent and Young Female Patients with Suspected or Confirmed Diagnosis of Endometriosis by Laparoscopy.

Author, Year	No. Pat.	Age (Years)	Method of Final Diagnosis	Clinical Presentation (No, % of Patients)
Case series				
Bai (2002)[58]	39	14-21	Laparoscopy/laparotomy	Chronic pelvic pain (11, 27%) Acute pelvic pain (8, 21%) Palpable pelvic mass (8, 21%) Dysmenorrhea (7, 18%) Infertility (1, 3%)
Vicino (2010)[43]	38	≤ 21	Laparoscopy	Pelvic pain (38, 100%)
Tandoi (2011)[44]	57	16-21	Laparoscopy/laparotomy	Dysmenorrhea (43, 75%) Chronic pelvic pain (21, 37%) Dyspareunia (13, 23%) Dyschezia (3, 5.3%) Menometrorrhagia (1, 1.7%)
Unger (2011)[29]	3	13-16	Laparoscopy	Severe pelvic pain (3, 100%)
Yeung (2011)[60]	17	12-19	Laparoscopy	Dysmenorrhea (14, 82.4%) Dyschezia (13, 76.5%) Chronic Pelvic pain (13, 76.5%) Painful exercise (12, 70.6%) Intestinal cramping (10, 58.8%) Bladder pain and tender exam (9, 52.9%) Constipation (7, 41.2%) Dyspareunia (3, 17.6%)
Yang (2012)[30]	63	12-20	Laparoscopy/laparotomy	Cyclic pelvic pain (45, 71.4%) Acute abdominal pain (19, 30.1%) Gastrointestinal dysfunction (19, 30.1%) Chronic pelvic pain (13, 20.6%) Irregular menses (5, 7.9%) Dyspareunia (1, 1.6%)
Lee (2013)[45]	35	≤ 20	Laparoscopy	Pelvic pain (27,77%) Incidentally (8, 23%)
Ozyer (2013)[49]	63	17-24	Laparoscopy	Chronic pelvic pain (28, 44%) Infertility (15, 24%) Incidentally (8, 13%) Dysmenorrhea (11, 8%)
Andres (2014)[61]	21	13-20	Laparoscopy	Dysmenorrhea (17, 80.9%) Incapacitating dysmenorrhea (7, 33.3%) Chronic pelvic pain (7, 33.3%) Deep dyspareunia (7, 33.3%) Cyclic bowel symptoms (3, 14.2%) Infertility (1, 4.7%)
Smorgick (2014)[47]	86	≤ 22	Laparoscopy/laparotomy	Pelvic pain (70, 81.4%) Dyspareunia (46, 53.5%) GI symptoms (15, 17.4%) GU symptoms (10, 11.6%) Infertility (2, 2.3%)
Dun (2015)[11]	25	10-21	Laparoscopy	Dysmenorrhea (16, 64%) Abnormal/irregular uterine bleeding (15, 60%) GI symptoms (14, 56%) GU symptoms (13, 52%) Menorrhagia (11, 44%)
Audebert (2015)[31]	55	12-19	Laparoscopy	Dysmenorrhea (53, 96.4%) Chronic pelvic pain, dyspareunia, acute pain, and/or dyschezia (47, 85.4%) Infertility (5, 9%)
Fong (2017)[46]	45	14-25	Laparoscopy	Mild dysmenorrhea (20, 44.5%) Severe dysmenorrhea (18, 40%) Noncyclical pain (2, 4.4%) Menorrhagia (2, 4.4%)
Matalliotakis (2017)[63]	55	13-21	Laparoscopy	Dysmenorrhea (45, 81%) Pelvic pain (40, 72%) Infertility (6, 11%)
Al-Jefout (2018)[27]	20	15-21	Laparoscopy	Chronic pelvic pain (CPP) refractory to NSAIDs and hormonal therapy (20, 100%) Cold intolerance (14, 75%) Severe CPP with VAS ≥ 7 (14, 70%) Abnormal uterine bleeding (7, 35%)
Stochino (2020)[37]	32	< 20	Laparoscopy	Dysmenorrhea (30, 93.7%) Deep dyspareunia (19, 76%) Chronic pelvic pain (23, 71.9%) Defecation pain (10, 31.2%) Constipation (9, 28.1%) Diarrhea (8, 25%)

(*continued on next page*)

Table 2 (*continued*)

Author, Year	No. Pat.	Age (Years)	Method of Final Diagnosis	Clinical Presentation (No, % of Patients)
Martire (2020)[26]	36	12-20	US	Dysmenorrhea (31, 86.1%) Heavy menstrual bleeding (20, 55.5%) Dyspareunia (8, 22.2%) Chronic pelvic pain (5, 13.9%) Dyschezia (5, 13.9%) Functional bowel symptoms (4, 11.1%) Dysuria (3, 8.3%)
Martire (2023)[16]	131	12-25	US	Dysmenorrhea (131, 100%) Heavy menstrual bleeding (80, 61.1%) Dyspareunia (71, 54.2%) Dischezia and/or bowel functional symptoms (58, 44.3%) Dysuria (13, 9.9%)
Cross-sectional study				
Ragab (2015)[32]	56	15.2 (mean age)	US, MRI	Severe dysmenorrhea refractory to NSAIDs and hormonal therapy (56, 100%) GI symptoms (27, 48.2%) GU symptoms (15, 26.8%)
DiVasta (2018)[18]	295	8-18	Laparoscopy	Nausea associated with pain (130, 69.5%) General acyclic pelvic pain (194, 65.8%) Severe dysmenorrhea (186, 63.1%) Moderate dysmenorrhea (86, 29.2%) Vomiting associated with pain (45, 24.6%) Mild dysmenorrhea (20, 6.8%)
Case-control study				
Khashchenko (2023)[25]	90	15-17	Laparoscopy	Dysmenorrhea moderate-severe (88, 97.8%) Dysmenorrhea persistent to NSAIDs (86, 95.6%) Dysmenorrhea at menarche (57, 63.3%) GI symptoms (35, 38.9%) Heavy menstrual bleeding (31, 34.4%) GU symptoms (22, 22.4%)
Cohort study				
Roman (2010)[59]	20	14-19	Laparoscopy	Dysmenorrhea (16, 80%) Nonmenstrual pelvic pain (4, 20%)
Wuest (2023)[34]	144	15-24	Clinically confirmed diagnosis	Dysmenorrhea (133, 92.4%) Dyspareunia Noncyclic pain Dysuria, dyschezia
Total	**1426**	**8-25**	-	**Dysmenorrhea (1182, 82.9%)** **Pelvic pain (527/1227, 43%)** **Gastrointestinal symptoms (233/1227, 19%)** **Abnormal menstrual bleeding (257, 18%)** **Dyspareunia (168/1227, 13.7%)** **Genito-urinary symptoms (85/1282, 6.6%)**

GI: gastrointestinal; GU: genitourinary; VAS: visual analogue scale; MRI: magnetic resonance imaging; NSAIDs: nonsteroidal anti-inflammatory drugs.

with endometriosis, such as gastrointestinal manifestations and other vague abdominal symptoms. Attention should be given to the potential bias that may be implicit when addressing dyspareunia. In early adolescence, a higher number of presexually active girls results in a lower percentage of dyspareunia being reported, as shown in Martire et al.[26] however, sexually active teenagers appear to have more severe dyspareunia than do older women.[34]

Martire's 2020 and 2023 results[16,26] reveal that although dysmenorrhea was considered an indication for US examination in 10.4% of cases, the symptom was self-reported by 54.4% of patients when interviewed, making it the most common symptom. The 2023 study further found that patients reported severe dysmenorrhea only when specifically questioned about pelvic pain and asked to score their symptoms using the Visual Analog Scale (VAS). These findings suggest not only an underestimation of endometriosis symptoms by adolescents, who may perceive dysmenorrhea as a natural aspect of menstruation but also by general practitioners. Both articles underscore dysmenorrhea as a reliable indicator of endometriosis, emphasizing the need to recognize it in adolescents as a warning sign. The studies highlight the crucial need for actively inquiring about this symptom to ensure accurate diagnosis and appropriate management.

The results demonstrated by Al-Jefout et al.[27] suggest a potential link between chronic pain conditions, such as endometriosis, and a higher likelihood of anxiety-related symptoms, including cold intolerance.

While symptoms may align closely with the existence of endometriosis, they do not necessarily correspond to the stage or severity of the disease. The proposition that has been put forward suggests that endometriosis may be characterized as a "progressive" condition, as proposed by Brosens et al.[35] Prior studies addressing noninvasive endometriosis diagnosis in adolescents[36] revealed that the majority of adolescents are diagnosed with Stage I endometriosis. Our study reinforces these observations, with most laparoscopically confirmed cases in the lower ASRM stages.

Stochino's findings[37] suggest an age-related increase in endometriosis severity, with adolescents (<20 years) hav-

Table 3
US Findings in Adolescent and Young Female Patients with Clinically Suspected Endometriosis and US Findings in Patients Laparoscopically Diagnosed with Endometriosis.

US Findings in Patients with Clinically Suspected Endometriosis				
Author, Year	No. Patient	Age Range	US Method/Device	US Findings (No Patients, %)
Ragab (2015)[32]	220	NR	Transabdominal probe	**Positive US findings (56, 25.4%)**
Martire (2020)[26]	205*	12-20	Voluson E6 or E8 device with transvaginal/transrectal probe	**≥1 US sign of endometriosis** (36, 17.6%) Negative posterior sliding sign (18, 6.7%) Adnexal adhesions (18, 6.7%) DIE (10, 3.7%) Endometrioma (22, 8,1%)
Martire (2023)[16]	304**	12-25	Voluson E6 or E8 or E10 device with transvaginal/transrectal probe	**≥1 Typical US sign of pelvic endometriosis or adenomyosis** (131, 43.1%) Posterior DIE (70, 18.9%) Anterior DIE (1, 0.3%) Endometrioma (54, 14.5%) Adenomyosis (67, 18.1%) Adhesions (15, 13.7%)
Total of patients with clinically suspected endometriosis	**729**	12-25	-	**223 (30.6%) ≥ 1 sign of endometriosis in US** DIE (81/167, 48,5%) Endometrioma (76/167, 45.5%) Adenomyosis (67/167, 40.1%) Adhesions (33, 19.8%)
US findings in patients laparoscopically diagnosed with endometriosis				
Yang (2012)[30]	63	12-20	NR	Pelvic mass (55, 87.30%) Genital tract malformations (15, 23.8%)
Audebert (2015)[31]	55	12-19	NR	Pelvic mass (23, 41.8%) Mullerian abnormality (4, 7.3%)
Fong (2017)[46]	42	14-25	NR	Bilateral ovarian cysts (18, 42.9%) Unilateral ovarian cyst (23, 54.8%)
Al-Jefout (2018)[27]	20	15-21	NR	Ovarian mass (8, 40%) Endometrioma (3, 15%)
Khashchenko (2023)[25]	90	15-17	Vivid-q, GE HEALTHCARE, with transabdominal probe	Peritoneal endometriosis (3, 3.3%)
Total of patients with laparoscopically diagnosis of endometriosis	**270**	12-25	-	**Pelvic mass/cyst: 127 (47%)** **Endometrioma: 3 (1.1%)** **Peritoneal endometriosis (1.1%)**

NR: not reported; DIE: deep infiltrating endometriosis; US: ultrasound; PE: peritoneal endometriosis.
* 24.1% of the adolescent population were referred to the US unit for a routine scan in the absence of any symptoms or clinical suspicions (270 × 24.1% = 65; 270 - 65 = 205). Since no asymptomatic teenager had endometrial signs in ultrasound, 65 adolescents were excluded from the analyses.
** 18.1% of the teenagers had routine examination referrals for the US, meaning that endometriosis was not suspected by the clinician in these cases. 67 teenagers were excluded from our analyses since all endometriotic abnormalities had been identified in symptomatic patients.

ing a mean disease stage of II. Furthermore, in the studies by DiVasta and Martire et al.[16,18,26] no cases of advanced disease were diagnosed by laparoscopy or ultrasound, respectively, corroborating previous results mentioned. This is consistent with published data regarding the staging of endometriosis.[38-42]

An exception is observed in five studies,[30,43-46] which report a large proportion of patients with endometriosis Stage III and IV. This advanced-stage prevalence may be attributed to complex cases treated in tertiary centers, population bias where inclusion criteria was based on the presence of endometrioma (with an immediate higher stage), delayed healthcare seeking, traditional medicine use, and the acceptance of surgery only when pelvic masses are evident. Fong's findings[46] suggest that older age (82.3% of women aged 21-25 years), higher prevalence of ovarian endometriomas (a marker of extensive disease), and selection bias (retrospective nature of the study) contributed to advanced-stage overrepresentation. Importantly, the majority of cases with higher ASRM stages in adolescents are due to ovarian endometriomas (compared with extensive peritoneal or adhesive disease). Lee et al.[45] reported only cases of Stage III and IV since the population included were adolescent females who underwent surgery for endometrioma, a lesion frequently associated with advanced endometriosis, a condition that often requires surgical intervention.

Endometriosis in its early stages may be associated with more metabolically active lesions, possibly associated with more painful symptoms, as opposed to larger, more fibrotic lesions. Wuest et al.[34] observed in their study that females younger than 24 years old with endometriosis had higher visual analogue scale scores for dysmenorrhea and non-cyclic pelvic pain than women older than 24. Tandoi et al.[44] pointed out that young age represents a determinant for the recurrence of the disease, speculating that the younger the age of onset, the more aggressive form of endometriosis. Also, Smorgick et al.[47] demonstrated that the occurrence of daily pelvic pain was found to be more common among women with early-stage endometriosis.

US Findings

Adolescent females undergoing US had an average age of 17.3 years, reflecting late adolescence. This aligns with increased sexual activity, contraception-seeking behavior, and gynecological consultations. Notably, only eight of 26 articles provided detailed US findings, even though the majority of articles mentioned its use.

Only 30.6% of the adolescents evaluated by transvaginal/transrectal/transabdominal ultrasound without laparoscopy showed signs of endometriosis, possibly due to challenges in detecting small lesions in young patients.

Table 4
Pelvic MRI Findings in Adolescent and Young Female Patients with Clinically and/or Imagological Suspected Signs of Endometriosis.

Pelvic MRI Findings of Endometriosis						
Author, Year	No. Pat.	Age (Years)	Protocol	MRI Machine	MRI Sequences	MRI Findings (No Patients, %)
Ragab (2015)[32]	22	15.2 (mean age)	Clinical and sonographic suspicion of endometriosis. After refusing laparoscopy.	NR	NR	Findings of endometriosis (17, 77.3%)
Millischer (2023)[33]	308	12-20	After a recorded clinical history where severe dysmenorrhea was reported.	1.5T MRI machine (Sonata; Siemens, Erlangen, Germany)	2 and 3 dimensional T2WI; T1WI with/without fat suppression; cine MRI	**Findings of endometriosis** (121, 39.3%): Isolated OMA (14, 11.6%) Isolated DIE (96, 79.3%) DIE and OMA (11, 9.1%) No visible lesion (187, 60.7%) **Type of endometriosis among 121 patients:** OMA (25, 20.7%) Retrocervical lesions (106, 87.6%) Rectosigmoid lesions (4, 3.3%) Associated adenomyosis (21, 17.4%) Uterine contractions (39, 32.2%)
Khashchenko (2023)[25]	90	15-17	After clinical history and US imaging recorded in patients with laparoscopically kdiagnosis of PE	GE Signa Excite 1.5T and GE Signa Architect 3.0T MRI systems	T2WI with slice thickness 0,3-0,6cm; T1WI and T1FS; diffusion weighted mode	**Peritoneal endometriosis** (71, 78.9%): Uterosacral ligament (39.4%) Parametrial tissue (38%) Along the ovarian capsule (35.2%) Paraovarian tissue (29.6%) Peritoneum and tissue of the Douglas pouch (25,4%) Posterior leaf of broad ligament (18.3%) Paracervical tissue (5.6%)
Total	**420**	12-20				**209 (49.8%)**

NR: not reported; OMA: ovarian endometrioma; DIE: deep infiltrating endometriosis; PE: peritoneal endometriosis; T2WI: T2 weighted images; T1W1: T1 weighted images; T1FS: T1 weighted fat-saturated image.

Unfortunately, not every study specified which probe was used.

Transvaginal ultrasonography is the preferred and most widely method used to diagnose endometriosis with standardized methods to describe the appearance of endometriosis using this sonography method.[48] Therefore, having TVUS, transabdominal US and transrectal US different diagnostic capacities, results using different US techniques should be interpreted carefully.[48] It's also crucial to note that adolescents who are not sexually active may find transvaginal US uncomfortable and may decline it; in these situations, transabdominal or transrectal US may be the only options accessible.

Despite the low percentage of positive sonographic signs encountered, especially in cases of superficial endometriosis, it should be reinforced that even with normal US findings in adolescents, the disease should be taken into consideration. Experienced sonographers with the ability to accurately diagnose endometriosis in this age group should be involved in the diagnosis.

Dysmenorrhea (86.1%) and dyspareunia (22.2%) were the most frequently reported symptoms by Martire et al.[16] that were linked to ultrasound findings for endometriosis. In the younger age group (12 to 16 years old), there was a lower prevalence of posterior DIE, endometrioma, and adenomyosis compared with the oldest group (17 to 20 years old). Martire's studies[16,26] highlight the prevalence of posterior compartment involvement in adolescent patients with endometriosis, contrasting with minimal reports in the anterior compartment, where only one lesion was reported. These results are consistent with the ones found by Ozyer[49] and Millischer.[33] This anatomical distribution supports the retrograde menstruation theory in this population, explaining the preference for lesions in Douglas's pouch.[50]

Our results suggest a complex landscape regarding the accuracy of ultrasound in diagnosing endometriosis in young females. Furthermore, due to the inconsistently reported data and the bias introduced by selection criteria, reliable data on the US findings of endometriosis in this population is clearly lacking.

MRI Findings

In two of the three studies included, MRI seems to be a promising diagnostic tool, even for patients who previously had normal ultrasounds. Results should be interpreted carefully, as we are not aware of how the previous US was performed (transvaginal/transabdominal approach, experienced sonographers) and one study focused on PE. MRI provides accurate insights into various forms of endometriosis and proves informative in assessing the extent of organ involvement, the presence of lesions away from the transvaginal ultrasound field, and the severity of adhesive processes.[51,52] Khashckenko et al.[25] corroborate the superior diagnostic accuracy of MRI over ultrasound (US) for detecting PE in adolescents (even though results start to look promising for the US detection of these lesions).[51,53]

Millischer et al.[33] revealed an age-dependent increase in the prevalence of MRI-visible endometriosis, particularly among adolescents with severe dysmenorrhea, confirming

that endometrioma and/or DIE can be observed in a large number of adolescents. Caution is warranted due to the potential overestimation of DIE lesions, given the recognized rate of false positives in MRI, even when administered by trained radiologists.

Despite the fact endometriosis has been found, as reported by Ragab et al.[32] those findings are not adequately clarified or discriminated.

MRI excels at identifying lesions, particularly in the posterior compartment (pouch of Douglas and uterosacral ligaments), offering multi-plane assessment and retrospective image review for comprehensive preoperative evaluation. Despite its benefits, MRI is costlier, less accessible and lacks real-time dynamic observation. In contrast, ultrasound, particularly transvaginal ultrasound (TVUS), offers real-time dynamic observation, being useful for more than just diagnosis; by considering the real-time discomfort and movement of the structures, it can provide insight into the presence of adhesions and obliteration of the pelvic pouches. Recent research has highlighted the enhanced role of transvaginal ultrasound in detecting superficial endometriosis lesions in adults and a similar accuracy in detecting ovarian endometriomas and deep endometriosis involving the rectosigmoid, compared to MRI.[51,52] Analysis of specific-site tenderness and ovary mobility has shown significant negative predictive value when absent, indicating their potential as diagnostic markers.[52] Nonetheless, TVUS's efficacy hinges on operator skill and may present challenges for presexually active young adolescents. Despite these disparities, both MRI and ultrasound play pivotal roles in endometriosis management, each complementing the other with distinct advantages and limitations.

Limitations

This systematic review notes some limitations: English-only searches, a small sample size ($n = 26$), and varied "adolescent" definitions lead to population heterogeneity. The study conducted by Sawyer et al.[21] defined the adolescent population between 10 and 24 years old. However, it is known that this investigation led to some disagreement among health professionals.[54,55] Scarce publications on ultrasound and MRI limit understanding of their role in diagnosing endometriosis; furthermore, some articles didn't describe the US probe used, and in some a transabdominal approach was used, with lesser accuracy for diagnosis. Not all studies reported their results clearly according to the IDEA consensus statement as to what constitutes features of endometriosis on ultrasound. Also, the literature mainly comprises case series, offering low-grade evidence. Laparoscopic challenges in diagnosing subtle atypical lesions, such as those that are clear, white, or red, being more common, and are more likely to be missed during surgery, even by experienced surgeons, adding complexity. This means that even in reports with laparoscopically confirmed endometriosis, the population might be truly underrepresented. Selection bias comes from predominantly including adolescents with prior diagnoses. The suitability of ASRM classification is uncertain in this population and data heterogeneity prevents the performance of a meta-analysis.

Strengths

While an increasing number of papers have addressed endometriosis in adolescence in recent years, this systematic review represents the first comprehensive systematic review focused on noninvasive diagnostic methods for endometriosis in this specific population, with a high number of adolescents included from many different countries. The study's strength lies in its meticulous methodological design, with a registered a priori protocol guarding against selective reporting and substantial deviations from the original plan. Despite variations in age groups, outcome measures, and follow-up moments in the published literature, the study provides the most precise overview of the current knowledge on diagnosing endometriosis in the adolescent population. Promisingly, the majority of studies in this review were classified as low risk of bias, contributing to the robustness of the findings.

Future Research

Future studies should focus on identifying disease markers, refining the quality and utility of transvaginal ultrasound, and increasing the role of magnetic resonance imaging (MRI). Additionally, patients, general practitioners, and pediatricians should be made more aware of endometriosis for a better diagnosis, but even more important for better pain management and quality of life. Predictive algorithms for the disease stage, such as questionnaires that evaluate a woman's medical, obstetric, and family history as well as her symptom pattern, should be emphasized. Adolescents with menstrual conditions like dysmenorrhea and heavy menstrual bleeding experience significant impacts on their school, work, sports, and social lives, as well as their relationships and struggle to articulate their needs, focusing instead on symptom experiences. The lack of understanding and negative attitudes from peers, especially boys, exacerbate their emotional distress.[56] On the other hand, parents often prioritize obtaining a diagnosis.[57] To address these issues, a population-based survey should be conducted to quantify unmet needs of this adolescents and young women and improve support and care.

Continued validation and wider implementation of these algorithms may help cut down on pointless surgeries, particularly in cases where patients with severe symptoms and advanced disease who are not responding to current treatments might benefit more from surgery. Research on imaging methods for diagnosing endometriosis in adolescents is vital for improving diagnostic accuracy. Advances in transvaginal ultrasound criteria and additional techniques show promise.

Conclusion

This systematic review has successfully identified patterns that can offer valuable insights for clinicians when assessing adolescent patients with pelvic pain. Dysmenorrhea and persistent pelvic pain were the most frequently reported symptoms, while US and MRI appear to offer valuable information for the disease's diagnosis when performed by qualified radiologists and sonographers. Posterior DIE is also identified in this population, and an-

terior compartment DIE seems rare. Furthermore, adolescents seem to experience severe pain more frequently than older women. The great number of different pain symptoms and low-stage lesions, based on the ASRM classification, reported in adolescents aligns with the hypothesis that endometriosis is a progressive disease. The review underscores the importance of noninvasive endometriosis diagnosis in adolescents, advocating for careful consideration of surgical interventions when imaging is normal. This represents an important step forward in understanding and managing endometriosis in adolescents.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Author Contributions

All authors contributed to the design of this review. IO and PP developed the search strategy with the help of JB. After the final search, IO was the first reviewer for article screening. PP and JB were the independent second and third reviewers for article screening. IO and PP contributed to data analysis, interpretation, and writing. JB contributed to data interpretation, reviewing the article, and approving the final version.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jpag.2024.07.005.

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