Prevalence of deep and ovarian endometriosis in women attending a general gynecology clinic: prospective cohort study

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CONTRIBUTION

What are the novel findings of this work?
This is the first large prospective study to investigate using a non-invasive approach the prevalence of endometriosis in women with a wide range of complaints attending a gynecological outpatient clinic.

What are the clinical implications of this work?
We found that deep pelvic endometriosis was much more prevalent than thought previously. It is therefore important that effective non-invasive diagnostic tests are offered routinely to women during their initial outpatient visit to facilitate timely diagnosis and effective treatment of this often-debilitating disease.

ABSTRACT

Objectives To assess using transvaginal ultrasound the prevalence of deep and ovarian endometriosis in premenopausal women attending a general gynecology clinic. We also investigated whether the presence of endometriosis was associated with various demographic factors and other pelvic abnormalities.

Methods This was a prospective observational cohort study carried out between February 2019 and October 2020. Consecutive premenopausal women who attended our general gynecology clinic underwent pelvic ultrasound examination, performed by a single experienced operator. Pregnant women and those with a history of hysterectomy or oophorectomy were excluded. The primary outcome was the prevalence of deep and/or ovarian endometriosis.

Secondary outcomes were the anatomical distribution of endometriotic lesions and the association of endometriosis with demographic characteristics and various pelvic abnormalities, which were analyzed using logistic regression and multivariable analysis.

Results A total of 1026 women were included in the final study sample, of whom 194 (18.9% (95% CI, 16.6–21.4%)) had sonographic evidence of deep and/or ovarian endometriosis. Of the 194 women diagnosed with endometriosis, 106 (54.6% (95% CI, 47.4–61.8%)) were diagnosed with endometriotic nodules only, 26 (13.4% (95% CI, 9.0–19.0%)) with ovarian endometriomas only, and 62 (32.0% (95% CI, 25.5–39.0%)) women had evidence of both. There was a total of 348 endometriotic nodules in 168 women, located most frequently in the retrocervical area (166/348; 47.7% (95% CI, 42.4–53.1%)), uterosacral ligaments (96/348; 27.6% (95% CI, 23.0–32.6%)) and bowel (40/348; 11.5% (95% CI, 8.3–15.3%)). Multivariable analysis found significant positive associations between endometriosis and both adenomyosis (odds ratio (OR), 1.72 (95% CI, 1.10–2.69); P = 0.02) and pelvic adhesions (OR, 25.7 (95% CI, 16.7–39.3); P < 0.001), whilst higher parity (OR, 0.44 (95% CI, 0.24–0.81); P = 0.03) and history of Cesarean section (OR, 0.18 (95% CI, 0.06–0.52); P = 0.002) were associated with a lower occurrence of endometriosis. A total of 75/1026 women (7.3% (95% CI, 5.8–9.1%)) underwent laparoscopy within 6 months of pelvic ultrasound examination. There was very good agreement between ultrasound and surgical findings, with a kappa value of 0.84 (95% CI, 0.69–0.99).

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ORIGINAL PAPER

Conclusions *Deep and/or ovarian endometriosis was present in nearly one in five women attending a general gynecology clinic. There were significant positive associations with adenomyosis and pelvic adhesions and negative associations with higher parity and previous Cesarean section. © 2023 The Authors. Ultrasound in Obstetrics & Gynecology published by John Wiley & Sons Ltd on behalf of International Society of Ultrasound in Obstetrics and Gynecology.*

INTRODUCTION

Endometriosis is an estrogen-dependent condition, defined as the presence of ectopic endometrial-like tissue[1] and classified as superficial, ovarian or deep-infiltrating[2]. Women with endometriosis often suffer from infertility and severe pelvic pain, which can be debilitating and have a significant adverse effect on quality of life[3]. The annual national economic burden of endometriosis has been reported as US\$15.58 billion in the UK and US\$78.05 billion in the USA[4].

To determine the real socioeconomic burden of endometriosis and to allocate appropriate healthcare resources for this disease, it is important to know its prevalence. The statistic usually cited for the prevalence of endometriosis in premenopausal women is 10%, although the most frequently referenced paper is from 1997, before standardized diagnostic criteria for this condition existed[3]. Most other studies have established the prevalence among women undergoing surgery[5,6], and their figures vary from 3.7% to 81.3%. The cause of this discrepancy is likely to be multifactorial, but influenced largely by the indication for surgery and highly selected study populations. The true prevalence is therefore unknown.

Until recently, histopathological examination of lesions excised during surgery was considered the reference standard for diagnosing endometriosis[7], but this introduces a selection bias as not all patients require surgery, and tissue samples can be damaged by heat during acquisition, preventing diagnosis. False-negative results can also occur, particularly when surgeons are insufficiently experienced in the laparoscopic diagnosis of endometriosis[8,9]. Transvaginal ultrasound (TVS) has emerged as an alternative diagnostic tool for deep and ovarian endometriosis, and its diagnostic accuracy is now deemed similar to that of laparoscopy[10]. The main advantage of an ultrasound-based diagnosis is that it offers the opportunity to diagnose endometriosis in a less selected group of women compared with surgery.

Only four other published studies have tried to determine the prevalence of endometriosis using TVS[11–14]. One was limited by its retrospective design[11], the second was conducted with the primary objective of determining the prevalence of adenomyosis[12], the third included pregnant women only[13] and the fourth women with subfertility only[14]. This study aimed to determine the prevalence of deep and/or ovarian endometriosis in a large consecutive cohort of premenopausal women attending our general gynecology clinic, using ultrasound, and to investigate which demographic characteristics and other pelvic abnormalities were associated with endometriosis.

METHODS

Study setting and patient population

This prospective observational cohort study was conducted at University College London Hospital, London, UK between February 2019 and October 2020. All women who attended our general gynecology clinic and were seen consecutively by a single examiner were eligible for inclusion. Inclusion criteria were the ability to undergo TVS and aged 18–50 years. Exclusion criteria were previous hysterectomy or unilateral/bilateral oophorectomy, pregnancy and postmenopausal state (defined as at least 12 months of amenorrhea, which could not be attributed to hormonal treatment, breastfeeding or endocrine disorders). The examiner (P.C.) had received over 3 years of intensive full-time training in gynecological ultrasound, particularly the diagnosis of deep and ovarian endometriosis, at a tertiary endometriosis center, and had scanned over 4000 patients with various gynecological complaints and pathologies over that period of time. Ethical approval was granted by the Liverpool Central Research Ethics Committee (date of approval: 22 January 2019; reference: 19/NW/0050). The study was registered on the Research Registry website (unique identifying number: researchregistry4828).

Primary and secondary outcomes

The primary outcome of this study was the prevalence of endometriosis (deep and/or ovarian). Secondary outcomes were the association between demographic variables and deep and ovarian endometriosis; the anatomical distribution of endometriotic lesions; and the association of endometriosis with other acquired gynecological abnormalities. A further secondary outcome was the level of agreement between ultrasound and surgical diagnosis of endometriosis in a subgroup of women who underwent subsequent surgery.

Data collection and image acquisition

A detailed demographic and clinical history was obtained for all women and all data were stored in a secure hospital database (Viewpoint Bildverarbeitung GmbH, Munich, Germany). Demographic data included age, ethnicity, smoking status and body mass index (BMI)[15]. Clinical data included indication for attendance, menstrual history, gravidity, previous miscarriage, termination of pregnancy and ectopic pregnancy, parity, mode of delivery of previous pregnancy (spontaneous/instrumental vaginal delivery or Cesarean section), history of infertility, contraceptive use at the time of consultation and previous history of endometriosis. The latter was obtained either from ultrasound or surgical records at our hospital, or patient-reported history. Menstrual characteristics were defined

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as per the revised International Federation of Gynecology and Obstetrics (FIGO) criteria: regularity of menstrual bleeding (regular: shortest-to-longest cycle variation of up 7–9 days, depending on age; irregular: shortest-to-longest cycle variation exceeding 8–10 days, depending on age); frequency of menstrual bleeding (absent: amenorrhea; infrequent: > 38 days; normal: 24–38 days; frequent: < 24 days); duration of menstrual bleeding (normal: ≤ 8 days; prolonged: > 8 days)[16]. Infertility was defined as the failure to establish a clinical pregnancy after 12 months of regular, unprotected sexual intercourse due to disease or impairment of a person's capacity to reproduce either as an individual or with her partner[17].

Two- and three-dimensional TVS assessments were undertaken systematically using a 4–9-MHz probe (Voluson E8; GE Healthcare, Zipf, Austria), as described below. A transabdominal scan to assess the kidneys was performed using a 2–5-MHz probe (Voluson E8; GE Healthcare).

Endometriosis was diagnosed using the detailed approach specified by the consensus statement from the International Deep Endometriosis Analysis (IDEA) group[18]. This included a systematic assessment of the uterus, ovaries, Fallopian tubes, anterior and posterior compartments of the pelvis, and distal ureters. All endometriotic lesions and other pelvic abnormalities were described, measured and recorded. The pelvic organs were also examined for tenderness and mobility.

Endometrioma was diagnosed when well-defined and thick-walled ovarian cysts containing homogeneous low-level internal echoes (ground-glass appearance) were seen[19]. Functional hemorrhagic cysts were differentiated from endometriomas by their typical spider-web appearance[20]. When it was difficult to distinguish between the two, a repeat scan was performed 6 weeks later, by which time a functional hemorrhagic cyst would have resolved.

Endometriotic nodules were characterized as hypoechogenic, avascular, solid lesions with irregular outer margins, found in various locations including the abdominal wall, adnexa, bladder, bowel, rectovaginal septum, retrocervical area, uterosacral ligaments, uterovesical fold and vagina[2,18]. Figure 1 illustrates deep endometriotic lesions diagnosed on ultrasound in these various locations. Endometriotic nodules are often tender on palpation with
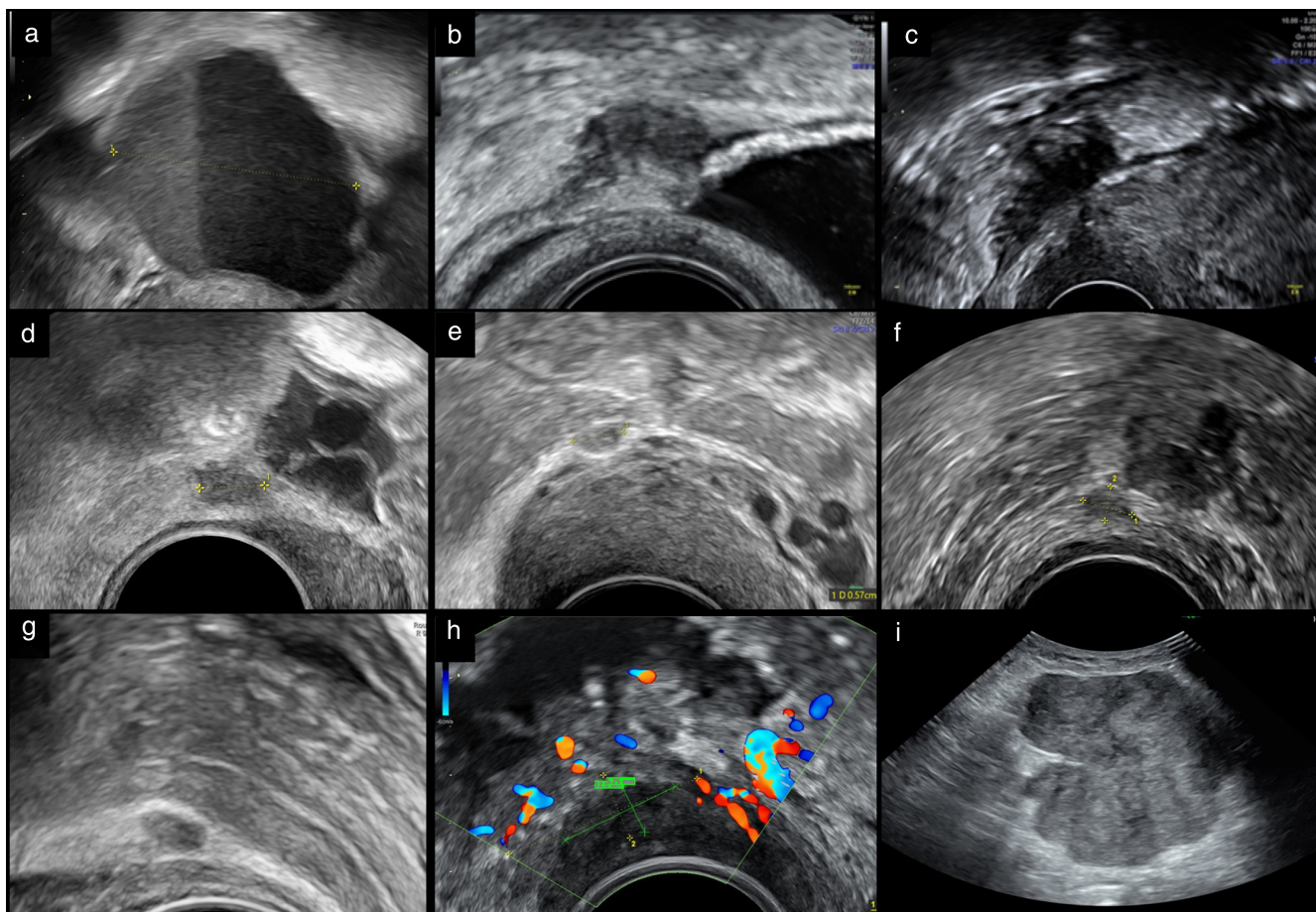

Figure 1 Two-dimensional transvaginal (a–h) and transabdominal (i) ultrasound images of deep endometriosis in various anatomical locations. (a) Ovarian endometrioma with mixed echogenicity demonstrating a blood-fluid level. (b) Bladder nodule located on bladder dome. (c) Hypoechogenic bowel nodule with irregular, spiked margins. (d) Isoechogenic nodule in retrocervical area. (e) Thickened uterosacral ligament containing an isogenic endometriotic nodule. (f) Adnexa/broad ligament with a hypoechogenic nodule. (g) Rectovaginal septum containing an isoechogenic endometriotic nodule. (h) Vaginal mucosa containing a hypoechogenic nodule. (i) Abdominal wall containing a well-demarcated but irregular nodule located between subcutaneous fat and abdominal fascia.

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the ultrasound probe, and the pelvic organs are found frequently to be fixed and tethered to each other at the site of these nodules.

Endometriomas and nodules were measured in three orthogonal planes and the mean of all three measurements was taken as the size of the lesion. Adhesions involving the pelvic organs and obliteration of the pouch of Douglas (POD) were diagnosed using the sliding organ sign[18] or the flapping sail sign in the case of filmy adhesions[21].

The following abnormalities were further assessed and noted: adenomyosis, fibroids, hydrosalpinges, hematosalpinges, cervical and endometrial polyps, non-endometriotic ovarian cysts, congenital uterine anomalies and accessory cavitated uterine malformations (ACUM). Adenomyosis and fibroids were diagnosed as per the Morphological Uterus Sonographic Assessment (MUSA) group consensus statement[22] and recent revisions in their definitions[23], polyps as per the International Endometrial Tumor Analysis (IETA) group consensus statement[24] and more recent literature[25], and ovarian cysts and hydro-/hematosalpinges using pattern recognition[26]. Congenital uterine anomalies were classified using the European Society of Human Reproduction and Embryology/European Society for Gynaecological Endoscopy (ESHRE/ESGE) classification system[27]. ACUM was diagnosed in accordance with recently described diagnostic criteria[28,29]. The kidneys were assessed transabdominally for hydronephrosis and other lesions such as renal cysts.

The presence or absence of endometriosis was noted in all women undergoing surgery within 6 months after TVS examination.

Sample size calculation and statistical analysis

Using an endometriosis prevalence of 10%[3], the required sample size for this study was calculated to be 865, to achieve a precision of 2% with a confidence level of 95%. Data were presented as mean ± SD if normally distributed or median (interquartile range) if non-normally distributed. The data distribution was determined by analysis of skewness and kurtosis. Proportions were calculated as percentages with corresponding 95% CI. Categorical variables were compared between groups using the chi-square test, except in the case of rarely occurring characteristics, for which Fisher's exact test was used. Continuous variables were compared between groups using the unpaired *t*-test if found to be normally distributed or the Mann–Whitney *U*-test otherwise.

Logistic regression and multivariable analysis were used to assess whether various demographic and clinical factors influenced the occurrence of deep or ovarian endometriosis. The size of the association was quantified by odds ratio, presented with corresponding 95% CI. For categorical variables, these represented the odds of endometriosis in each category relative to the odds in a baseline category. For continuous variables, the odds ratio represented the relative change in the odds of endometriosis for a given increase in each variable. Only factors showing some association with the presence of endometriosis on univariate

analysis ($P < 0.2$) were adjusted for in the multivariable analysis. A backwards selection procedure was performed to omit variables not independently associated with the presence of endometriosis (outcome). This involved removing non-significant variables, one at a time, until only factors associated with the outcome remained.

The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of TVS in the diagnosis of endometriosis were calculated based on the sample of women who underwent surgery. The agreement between TVS and laparoscopy in the diagnosis of endometriosis was assessed using the kappa statistic (κ), which measures the agreement over and above that which would be expected due to chance. This is measured on a scale ranging up to a maximum agreement of 1 (≤ 0.2, very poor agreement; 0.21–0.4, poor agreement; 0.41–0.6, moderate agreement; 0.61–0.8, good agreement; and 0.81–1.0, very good agreement)[30]. *P*-values of < 0.05 were considered statistically significant. Statistical analysis was performed using Stata version 15.1 (StataCorp., College Station, TX, USA).

RESULTS

During the study period, 2175 women were examined, of whom 1026 satisfied the inclusion criteria and formed the final study sample (Figure 2). The demographic and clinical characteristics of the study population are summarized in Table 1 and the indications for their visit in Table 2.
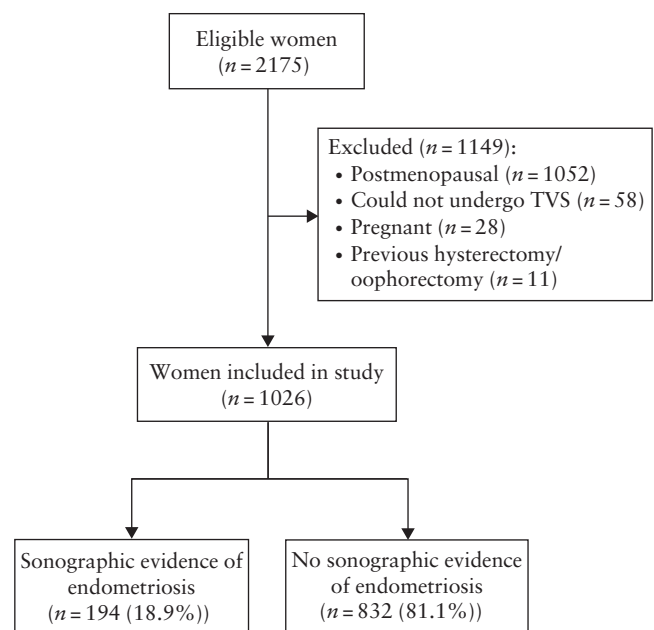

Figure 2 Flowchart summarizing inclusion, exclusion and diagnosis of women attending gynecology clinic during study period. TVS, transvaginal ultrasound.

Table 1 Demographic and clinical characteristics of 1026 study participants, according to presence or absence of endometriosis on transvaginal ultrasound

	Endometriosis		
Characteristic	Yes (n = 194)	No (n = 832)	P
Age (years)	36.5 ± 7.4	36.7 ± 8.2	0.69
Ethnicity			
Caucasian	104 (53.6)	448 (53.8)	0.95
Asian	28 (14.4)	108 (13.0)	0.59
Afro-Caribbean	23 (11.9)	130 (15.6)	0.18
Mixed/other	39 (20.1)	146 (17.5)	0.40
Body mass index* (kg/m²)	24.7 (21.7–28.3)	24.1 (21.0–28.9)	0.36
Smoking status†			
Non-smoker	125/184 (67.9)	586/747 (78.4)	0.003
Ex-smoker	40/184 (21.7)	106/747 (14.2)	0.012
Current smoker	19/184 (10.3)	55/747 (7.4)	0.19
Regularity of menstrual bleeding‡			0.26
Regular	146/187 (78.1)	563/760 (74.1)	
Irregular	41/187 (21.9)	197/760 (25.9)	
Frequency of menstrual bleeding			
Normal	131 (67.5)	509 (61.2)	0.10
Absent	7 (3.6)	72 (8.7)	0.02
Infrequent	7 (3.6)	61 (7.3)	0.06
Frequent	5 (2.6)	32 (3.8)	0.39
Variable	44 (22.7)	158 (19.0)	0.24
Duration of menstrual bleeding‡			
Normal	162/187 (86.6)	632/760 (83.2)	0.25
Prolonged	9/187 (4.8)	39/760 (5.1)	0.86
Variable	16/187 (8.6)	89/760 (11.7)	0.22
Contraceptive use			
None	139 (71.6)	546 (65.6)	0.11
Hormonal	37 (19.1)	196 (23.6)	0.18
Non-hormonal	18 (9.3)	90 (10.8)	0.53
Gravidity			
0	95 (49.0)	338 (40.6)	0.03
1	50 (25.8)	158 (19.0)	0.03
≥ 2	49 (25.3)	336 (40.4)	< 0.001
Parity			
0	130 (67.0)	452 (54.3)	0.001
1	34 (17.5)	138 (16.6)	0.75
≥ 2	30 (15.5)	242 (29.1)	< 0.001
History of infertility	42 (21.6)	114 (13.7)	0.006

Data are given as mean ± SD, *n* (%), median (interquartile range) or *n/N* (%). *Data missing for 552 women. †Data missing for 95 women. ‡Excluding 79 women with absent menstrual bleeding.

A total of 194/1026 (18.9% (95% CI, 16.6–21.4%)) women had evidence of deep and/or ovarian endometriosis on TVS examination, of whom 132 (68.0% (95% CI, 61.0–74.5%)) were diagnosed with endometriosis for the first time. The remaining 62/194 (32.0% (95% CI, 25.5–39.0%)) women had been diagnosed previously with endometriosis; 34/62 (54.8% (95% CI, 41.7–67.5%)) at laparoscopy and 28/62 (45.2% (95% CI, 32.5–58.3%)) on ultrasound.

Of the 194 women diagnosed with endometriosis, 106 (54.6% (95% CI, 47.4–61.8%)) had endometriotic nodules only, 26 (13.4% (95% CI, 9.0–19.0%)) had ovarian endometriosis only, and 62 (32.0% (95% CI, 25.5–39.0%)) had evidence of both deep endometriotic nodules and endometriomas.

A total of 125 endometriomas were identified in 88 women, with a median of 1 (range, 1–4) cyst per patient and a median size of 20.7 (range, 6.3–110.3) mm. The number of cysts in the left and right ovaries was not significantly different (70/125 (56.0%) *vs* 55/125 (44.0%), *P* = 0.18). In the 168 women with evidence of deep endometriosis, there was a total of 348 nodules, with a median of 2 (range, 1–7) per patient and a median size of 7.0 (range, 2.7–44.7) mm. The anatomical distribution of the nodules is listed in Table 3, and shows that they were located most frequently in the retrocervical area (166/348 (47.7% (95% CI, 42.4–53.1%)), uterosacral ligaments (96/348 (27.6% (95% CI, 23.0–32.6%)) and bowel (40/348 (11.5% (95% CI, 8.3–15.3%)).

Table 3 Anatomical distribution of 348 endometriotic nodules in 168 women

Location of endometriotic nodules	n (%)	95% CI (%)
Retrocervical area	166 (47.7)	42.4–53.1
Uterosacral ligament	96 (27.6)	23.0–32.6
Bowel	40 (11.5)	8.3–15.3
Adnexa	32 (9.2)	6.4–12.7
Vagina	5 (1.4)	0.5–3.3
Rectovaginal septum	3 (0.9)	0.2–2.5
Abdomen	3 (0.9)	0.2–2.5
Bladder/uterovesical fold	3 (0.9)	0.2–2.5

Table 2 Primary indication for attendance at general gynecology clinic, according to presence or absence of endometriosis on transvaginal ultrasound (*n* = 1026)

	Endometriosis				
	Yes (n = 194)		No (n = 832)		
Indication	n (%)	95% CI (%)	n (%)	95% CI (%)	P
Chronic pelvic pain	37 (19.1)	13.8–25.3	139 (16.7)	14.2–19.4	0.43
Dysmenorrhea	36 (18.6)	13.4–24.8	50 (6.0)	4.5–7.8	< 0.001
Abnormal uterine bleeding					
Intermenstrual bleeding	14 (7.2)	4.0–11.8	102 (12.3)	10.1–14.7	0.05
Heavy uterine bleeding and dysmenorrhea	25 (12.9)	8.5–18.4	53 (6.4)	4.8–8.3	0.002
Heavy uterine bleeding	22 (11.3)	7.3–16.7	155 (18.6)	16.0–21.4	0.02
Irregular menstrual bleeding	7 (3.6)	1.5–7.3	29 (3.5)	2.4–5.0	0.93
Infertility	5 (2.6)	0.8–5.9	20 (2.4)	1.5–3.7	0.88
Deep dyspareunia	2 (1.0)	0.1–3.7	26 (3.1)	2.1–4.6	0.11
Other	46 (23.7)	17.9–30.3	258 (31.0)	27.9–34.3	0.04

The association of endometriosis with demographic factors and gynecological abnormalities is shown in Tables 4 and 5. A statistically significant, positive non-linear relationship between age and the occurrence of endometriosis was seen (Figure 3). Current and ex-smokers had a significantly higher occurrence of endometriosis compared with non-smokers (Table 4). The frequency of endometriosis was twice as high in women with no or just one prior pregnancy compared to those with gravidity of two or higher, and over twice as high in nulliparous women compared to those with parity of two or more. Women with a history of infertility were almost twice as likely to have endometriosis than were those without infertility.

Compared to women without these diagnoses, adenomyosis, functional hemorrhagic cysts and renal tract abnormalities were associated with a significantly increased risk of concomitant endometriosis. Pelvic abnormalities known to be caused by endometriosis, including pelvic adhesions and dilated Fallopian tubes, were also significantly more common in women with endometriosis. After adjusting for age, BMI, history of infertility, frequency of menstrual bleeding, parity, smoking status, surgical termination of pregnancy, adenomyosis, dermoid cyst, dilated Fallopian tube, functional hemorrhagic cyst, pelvic adhesions and renal tract abnormality, our multivariable analysis showed that lower parity, adenomyosis and pelvic adhesions remained significantly associated with having endometriosis, while having had one or more Cesarean sections was negatively associated with endometriosis (Table 6). The equation for the logistic regression model was: $\text{logit}(P) = -2.38 - (0.22$ if parity is 1, 0.84 if parity ≥ 2, 0 if nulliparous$) - (0.90$ if one Cesarean section, 1.68 if ≥ 2 Cesarean sections, 0 if no Cesarean sections$) + (0.55$ if adenomyosis is present, 0 if absent$) + (3.25$ if pelvic adhesions are present, 0 if absent$)$, where P is the probability of endometriosis being present.

A total of 75/1026 (7.3% (95% CI, 5.8–9.1%)) patients underwent laparoscopy, of whom 15 (20.0% (95% CI, 11.7–30.8%)) were diagnosed with endometriosis at surgery. There was agreement between TVS and surgery findings in 71/75 (94.7% (95% CI, 86.9–98.5%)) cases, resulting in a κ of 0.842 (95% CI, 0.693–0.991), suggesting very good agreement between the two methods in detecting the presence or absence of endometriosis. In four women for whom there was disagreement between TVS and surgery findings, there was no evidence of endometriosis on ultrasound, but surgery found superficial endometriosis. The sensitivity, specificity, PPV, NPV and accuracy of TVS in detecting endometriosis were 73.3% (95% CI, 44.9–92.2%), 100% (95% CI, 94.0–100%), 100% (95% CI, 94.9–100%), 93.8% (95% CI, 86.6–97.2%) and 94.7% (95% CI, 86.9–98.5%), respectively, when using visual surgical findings as the reference standard. All 11/75 women with laparoscopic evidence of endometrioma or deep endometriotic nodules were also diagnosed on ultrasound, resulting in a sensitivity of 100% (95% CI, 71.5–100%) of TVS in diagnosing deep and ovarian endometriosis.

Table 4 Univariate analysis of association between demographic and clinical variables and presence of endometriosis on transvaginal ultrasound ($n = 1026$)

Variable	Endometriosis present (n/N (%))	OR (95% CI)	P
Age*			0.04
Linear term	—	9.09 (1.40–59.10)	
Squared term	—	0.73 (0.56–0.95)	
Ethnicity			0.50
Caucasian	104/552 (18.8)	1	
Asian	28/136 (20.6)	1.12 (0.70–1.78)	
Afro-Caribbean	23/153 (15.0)	0.76 (0.46–1.25)	
Mixed/other	39/185 (21.1)	1.15 (0.76–1.74)	
BMI (continuous)*†	—	1.09 (0.80–1.47)	0.59
BMI (categorical)†			0.19
18.5–24.9 kg/m^2	65/249 (26.1)	1	
< 18.5 kg/m^2	3/19 (15.8)	0.53 (0.14–1.88)	
25.0–29.9 kg/m^2	35/108 (32.4)	1.36 (0.83–2.22)	
30.0–34.9 kg/m^2	10/56 (17.9)	0.62 (0.29–1.29)	
35.0–39.9 kg/m^2	8/21 (38.1)	1.74 (0.69–4.39)	
≥ 40.0 kg/m^2	4/21 (19.0)	0.67 (0.22–2.05)	
Smoking status‡			0.01
Non-smoker	125/711 (17.6)	1	
Ex-smoker	40/146 (27.4)	1.77 (1.17–2.67)	
Current smoker	19/74 (25.7)	1.62 (0.93–2.82)	
Regularity of menstrual bleeding§			0.26
Regular	146/709 (20.6)	1	
Irregular	41/238 (17.2)	0.80 (0.55–1.18)	
Frequency of menstrual bleeding			0.01
Normal	131/640 (20.5)	1	
Absent	7/79 (8.9)	0.38 (0.17–0.84)	
Infrequent	7/68 (10.3)	0.45 (0.20–1.00)	
Frequent	5/37 (13.5)	0.60 (0.23–1.59)	
Variable	44/202 (21.8)	1.08 (0.74–1.59)	
Duration of menstrual bleeding§			0.43
Normal	162/794 (20.4)	1	
Prolonged	9/48 (18.8)	0.90 (0.43–1.90)	
Variable	16/105 (15.2)	0.70 (0.40–1.22)	
Gravidity			< 0.001
0	95/433 (21.9)	1	
1	50/208 (24.0)	1.13 (0.76–1.66)	
≥ 2	49/385 (12.7)	0.52 (0.36–0.76)	
Parity			< 0.001
0	130/582 (22.3)	1	
1	34/172 (19.8)	0.86 (0.56–1.31)	
≥ 2	30/272 (11.0)	0.43 (0.28–0.66)	
Contraceptive use			0.27
None	139/685 (20.3)	1	
Hormonal	37/233 (15.9)	0.74 (0.50–1.10)	
Non-hormonal	18/108 (16.7)	0.79 (0.46–1.35)	
Vaginal delivery¶			0.43
0	21/128 (16.4)	1	
1	19/131 (14.5)	0.86 (0.44–1.70)	
≥ 2	24/185 (13.0)	0.76 (0.40–1.43)	
Cesarean section¶			0.25
0	42/267 (15.7)	1	
1	16/106 (15.1)	0.95 (0.51–1.78)	
≥ 2	6/71 (8.5)	0.49 (0.20–1.21)	
Non-surgically managed miscarriage**			0.94
0	70/423 (16.5)	1	
1	21/119 (17.6)	1.08 (0.63–1.85)	
≥ 2	8/51 (15.7)	0.94 (0.42–2.08)	

Continued over.

Table 4 *Continued*

Variable	Endometriosis present (n/N (%))	OR (95% CI)	P
Surgically managed miscarriage**			0.36
0	87/536 (16.2)	1	
≥ 1	12/57 (21.1)	1.38 (0.70–2.71)	
Ectopic pregnancy**			0.58
0	94/569 (16.5)	1	
≥ 1	5/24 (20.8)	1.33 (0.48–3.65)	
Surgically terminated pregnancy**			0.10
0	76/462 (16.5)	1	
1	21/97 (21.6)	1.30 (0.75–2.25)	
≥ 2	2/34 (5.9)	0.31 (0.07–1.33)	
Medically terminated pregnancy**			0.50
0	89/521 (17.1)	1	
≥ 1	10/72 (13.9)	0.78 (0.39–1.59)	
History of infertility			0.006
No	152/870 (17.5)	1	
Yes	42/156 (26.9)	1.74 (1.10–2.58)	

*Odds ratios (OR) given for a 10-unit increase in predictor variable. †Data missing for 552 women. ‡Data missing for 95 women. §Excluding 79 women with absent menstrual bleeding. ¶Excluding 582 nulliparous women. **Excluding 433 nulligravid women. BMI, body mass index.

DISCUSSION

In this study, the prevalence of deep and/or ovarian endometriosis in women attending our general gynecology clinic was 18.9%. This is consistent with a recent study that reported an ultrasound-based prevalence of 21.8% in women undergoing their first assisted reproductive treatment, using the same diagnostic criteria as those in this study[14]. However, previous prospective ultrasound-based studies reported a much lower prevalence[12,13], between 4.9% and 6.4%. The difference is likely due to variation in patient populations, as those studies also included postmenopausal women[12] or only pregnant women[13], in whom diagnosis is difficult due to anatomical and phenotypical changes. Also, the diagnosis of endometriosis has evolved significantly since the earlier study[12]. The only other study measuring the prevalence of endometriosis using TVS was retrospective, reporting a prevalence of deep and ovarian endometriosis of 25% in women with symptoms suggestive of endometriosis[11]. Exclusion of asymptomatic women and those presenting with non-specific gynecological symptoms could explain the higher prevalence compared with this study.

Most other published studies describing endometriosis prevalence included highly selected groups of women, for example women undergoing laparoscopy for infertility[6,31,32], chronic pelvic pain[6,31,33–35], sterilization[5,6,31,36,37] or symptoms not typically associated with endometriosis[38,39]. The prevalence reported by these studies varies significantly, ranging from 3.7% to 81.3%. Differences in surgical indications and expertise, patient demographics and presenting symptoms could explain this variation[40].

Table 5 Univariate analysis of association between concomitant ultrasound diagnoses and presence of endometriosis on transvaginal ultrasound (*n* = 1026)

Diagnosis	Endometriosis present (n/N (%))	OR (95% CI)	P
Uterine fibroids			0.70
No	120/647 (18.5)	1	
Yes	74/379 (19.5)	1.07 (0.77–1.47)	
Adenomyosis			< 0.001
No	112/743 (15.1)	1	
Yes	82/283 (29.0)	2.30 (1.66–3.18)	
Pelvic adhesions			< 0.001
No	59/806 (7.3)	1	
Yes	135/220 (61.4)	20.10 (13.80–29.40)	
Non-endometriotic ovarian cyst			0.58
No	163/848 (19.2)	1	
Yes	31/178 (17.4)	0.89 (0.58–1.35)	
Simple benign ovarian cyst			0.22
No	181/934 (19.4)	1	
Yes	13/92 (14.1)	0.68 (0.37–1.26)	
Functional hemorrhagic cyst			0.002
No	181/995 (18.2)	1	
Yes	13/31 (41.9)	3.25 (1.56–6.75)	
Dermoid			0.05
No	191/983 (19.4)	1	
Yes	3/43 (7.0)	0.32 (0.10–1.04)	
Cystadenoma			1.00
No	191/1010 (18.9)	1	
Yes	3/16 (18.8)	0.99 (0.28–3.51)	
Fibroma*			—
No	193/1024 (18.8)	—	
Yes	1/2 (50.0)	—	
Ovarian cancer†			1.00
No	194/1022 (19.0)	—	
Yes	0/4 (0)	—	
Borderline ovarian cyst*			—
No	194/1024 (18.9)	—	
Yes	0/2 (0)	—	
Endometrial and cervical polyps			0.78
No	173/909 (19.0)	1	
Yes	21/117 (17.9)	0.93 (0.56–1.53)	
Polycystic ovaries			0.52
No	179/933 (19.2)	1	
Yes	15/93 (16.1)	0.81 (0.46–1.44)	
Dilated Fallopian tubes			< 0.001
No	181/1001 (18.1)	1	
Yes	13/25 (52.0)	4.91 (2.20–10.90)	
Major congenital uterine anomaly			0.93
No	190/1004 (18.9)	1	
Yes	4/22 (18.2)	0.95 (0.32–2.85)	
ACUM			1.00
No	193/1021 (18.9)	1	
Yes	1/5 (20.0)	1.07 (0.12–9.65)	
Renal abnormality			0.02
No	189/1016 (18.6)	1	
Yes	5/10 (50.0)	4.38 (1.25–15.30)	
Any abnormality			< 0.001
No	11/213 (5.2)	1	
Yes	183/813 (22.5)	5.33 (2.84–10.00)	

*No formal analysis performed due to low number of women with risk factor. †Unable to calculate odds ratio (OR), as all women in one group had the same outcome. ACUM, accessory cavitated uterine malformation.
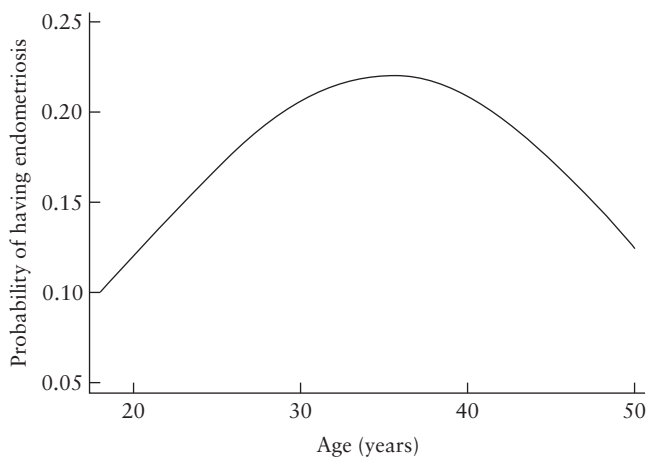
Figure 3 Fitted relationship between age and probability of having endometriosis, illustrating findings from univariate analysis.

Table 6 Multivariable analysis of demographic and clinical variables, concomitant ultrasound diagnoses and their association with endometriosis ($n = 1026$)

Variable	OR (95% CI)	P
Parity		0.03
0	1	
1	0.83 (0.43–1.56)	
≥ 2	0.44 (0.24–0.81)	
Cesarean section		0.002
0	1	
1	0.41 (0.18–0.92)	
≥ 2	0.18 (0.06–0.52)	
Adenomyosis		0.02
No	1	
Yes	1.72 (1.10–2.69)	
Pelvic adhesions		< 0.001
No	1	
Yes	25.7 (16.7–39.3)	

OR, odds ratio.

The few studies that have attempted to ascertain the true prevalence of endometriosis in an unselected population reported prevalences between 0.1% and 8.0%, which is much lower than that suggested by our findings[41]. They were, however, based on questionnaires, self-reported data and population-based integrated information systems, and would have excluded women with asymptomatic endometriosis, who are less likely to have undergone diagnostic tests compared with symptomatic women.

Our analysis of risk factors for endometriosis concurs with the existing literature in demonstrating a negative correlation between parity and endometriosis, meaning that pregnancy represents a protective factor for endometriosis[42].

In this study, women with one or more previous Cesarean section were less likely to have endometriosis, which is at odds with previous studies, in which a higher risk of endometriosis was noted in women with a history of Cesarean section[43,44]. This result was significant on multivariable analysis only after adjustments were made for the presence of pelvic adhesions. Adhesions were more common in women with a history of Cesarean section and their frequency increased with the number of previous Cesareans. However, adhesions after Cesarean section tend to form mainly in the anterior pelvic compartment, unlike those typically associated with endometriosis, which affect the ovaries and POD.

Pelvic adhesions form part of the disease process of endometriosis[18]. This study confirmed a strong positive correlation between the presence of pelvic adhesions and endometriosis. Identification of pelvic adhesions on ultrasound should, therefore, raise high suspicion of endometriosis, although they are not pathognomonic for endometriosis.

Our univariate analysis found a positive association between history of infertility and the presence of endometriosis, however it was no longer significant when adjusting for pelvic adhesions on multivariable analysis. Severe endometriosis is thought to affect fertility partly through distortion of functional anatomy caused by pelvic adhesions[45,46].

Similarly, functional hemorrhagic ovarian cysts were associated strongly with the presence of endometriosis on univariate analysis, but multivariable analysis suggested that this was due to confounding from pelvic adhesions. A recent study found that significant hemoperitoneum secondary to ruptured hemorrhagic cysts can trigger development of endometriotic deposits and pelvic adhesions[47]. That study and ours might suggest that hemorrhagic cysts are associated with an increased risk of endometriosis. Fluid from ruptured hemorrhagic cysts and retrograde menstruation often collects in gravity-dependent regions of the pelvis, usually the POD, so endometriotic nodules are more likely to develop in this area, as demonstrated by this study and others[13,48].

We found that 70.5% of women with endometrioma also had deep endometriotic nodules, which is comparable to the rate reported by other recent studies[13,49,50]. This is important because if ovarian endometriosis has been identified, deep endometriosis is likely to also be present, and should be searched for carefully. This can help to triage patients for surgery, as excision of deep endometriosis should be performed by expert surgeons[51].

This study concurred with the majority of previous studies[12,52–54] in demonstrating a positive correlation between adenomyosis and the presence of endometriosis. Both conditions are thought to share similar etiology, including uterine hyperperistalsis[55,56] and estrogen dependence[57].

The main strengths of this study are the prospective design, clearly defined diagnostic criteria and large consecutive sample size. All consultations and examinations were performed by a single examiner with extensive gynecological ultrasound experience, enabling a consistent approach to data collection and ultrasound examination, and eliminating interobserver variability.

The main limitation of this study is that the study population may not truly represent the general population, as women attending general gynecology clinics are more likely to be symptomatic and potentially suffer from

endometriosis. Furthermore, our general gynecology clinic could be over-representative of women with symptoms suggestive of endometriosis compared to general gynecology clinics elsewhere. However, the prevalence reported in this study is probably closer to the true prevalence in the general population than that described by previous studies, as TVS allows for the diagnosis of endometriosis in women not requiring surgery.

While an ultrasound-based diagnosis of endometriosis was considered inferior to a surgically established diagnosis before, this view has now shifted[10], supported by the very high agreement between our findings and laparoscopy. However, ultrasound cannot reliably detect superficial endometriosis, which is a limitation of this method. Then again, recent evidence has suggested that superficial endometriosis may just be a physiological phenomenon without clinical significance[58], in which case there would be little clinical benefit in establishing its prevalence.

In conclusion, this study found that deep and ovarian endometriosis was significantly more common in women attending our general gynecology clinic than the background population estimate of 2–10% quoted in the latest endometriosis guidelines[10]. In view of this, all symptomatic women attending gynecology clinics should be offered a detailed pelvic ultrasound scan to detect possible pelvic endometriosis and facilitate early and more effective treatment.

REFERENCES

1. Farquhar CM. Endometriosis. *BMJ* 2000; **320**: 1449.
2. International Working Group of AAGL, ESGE, ESHRE and WES, Tomassetti C, Johnson N P, Petrozza J, Abrao M S, Einarsson J I, Horne A W, Lee T T M, Missmer S, Vermeulen N, Zondervan K T, Grimbizis G, De Wilde R L. An international terminology for endometriosis, 2021. *Hum Reprod Open* 2021; **2021**: hoab029.
3. Ezkenazi B, Warner ML. Epidemiology of endometriosis. *Obstet Gynecol Clin North Am* 1997; **24**: 235–258.
4. Soliman AM, Yang H, Du EX, Kelley C, Winkel C. The direct and indirect costs associated with endometriosis: a systematic literature review. *Hum Reprod* 2016; **31**: 712–722.
5. Sangi-Haghpeykar H, Poindexter AN. Epidemiology of endometriosis among parous women. *Obstet Gynecol* 1995; **85**: 983–992.
6. Fauconnier A, Chapron C. Endometriosis and pelvic pain: epidemiological evidence of the relationship and implications. *Hum Reprod Update* 2005; **11**: 595–606.
7. Kuznetsov L, Dworzynski K, Davies M, Overton C, Guideline Committee. Diagnosis and management of endometriosis: summary of NICE guidance. *BMJ* 2017; **358**: 3935.
8. Griffiths AN, Koutsouridou RN, Penketh RJ. Rectovaginal endometriosis: a frequently missed diagnosis. *J Obstet Gynaecol* 2007; **27**: 605–607.
9. Leonardi M, Singh S, Murji A, Satkunaratnam A, Atri M, Reid S, Condous G. Deep endometriosis: a diagnostic dilemma with significant surgical consequences. *J Obstet Gynaecol Can* 2018; **40**: 1198–1203.
10. Becker CM, Bokor A, Heikinheimo O, Horne A, Jansen F, Kiesel L, King K, Kvaskoff M, Nap A, Peterson K, Saridogan E, Tomassetti C, van Hanegem N, Vulliemoz N, Vermeulen N; ESHRE Endometriosis Guideline Group. ESHRE guideline: endometriosis. *Hum Reprod Open* 2022; **2022**: hoac009.
11. Orlov S, Jokubkiene L. Prevalence of endometriosis and adenomyosis at transvaginal ultrasound examination in symptomatic women. *Acta Obstet Gynecolog Scand* 2022; **101**: 524–531.
12. Naftalin J, Hoo W, Pateman K, Mavrelos D, Holland T, Jurkovic D. How common is adenomyosis? A prospective study of prevalence using transvaginal ultrasound in a gynaecology clinic. *Hum Reprod* 2012; **27**: 3432–3439.
13. Bean E, Naftalin J, Horne A, Saridogan E, Cutner A, Jurkovic D. Prevalence of deep and ovarian endometriosis in early pregnancy: ultrasound diagnostic study. *Ultrasound Obstet Gynecol* 2022; **59**: 107–113.
14. Alson S, Jokubkiene L, Henic E, Sladkevicius P. Prevalence of endometrioma and deep infiltrating endometriosis at transvaginal ultrasound examination of subfertile women undergoing assisted reproductive treatment. *Fertil Steril* 2022; **118**: 915–923.
15. National Institue for Health and Care Excellence. Clinical Knowledge Summary: How should I confirm if a person is overweight or obese? https://cks.nice.org.uk/topics/obesity/diagnosis/identification-classification/.
16. Munro MG, Critchley HOD, Fraser IS. The two FIGO systems for normal and abnormal uterine bleeding symptoms and classification of causes of abnormal uterine bleeding in the reproductive years: 2018 revisions. *Int J Gynaecol Obstet* 2018; **143**: 393–408.
17. Zegers-Hochschild F, Adamson GD, Dyer S, Racowsky C, de Mouzon J, Sokol R, Rienzi L, Sunde A, Schmidt L, Cooke ID, Simpson JL, van der Poel S. The International Glossary on Infertility and Fertility Care. *Fertil Steril* 2017; **108**: 393–406.
18. Guerriero S, Condous G, Van den Bosch T, Valentin L, Leone FP, Van Schoubroeck D, Exacoustos C, Installé AJF, Martins WP, Abrao MS, Hudelist G, Bazot M, Alcazar JL, Gonçalves MO, Pascual MA, Ajossa S, Savelli L, Dunham R, Reid S, Menakaya U, Bourne T, Ferrero S, Leon M, Bignardi T, Holland T, Jurkovic D, Benacerraf B, Osuga Y, Somigliana E, Timmerman D. Systematic approach to sonographic evaluation of the pelvis in women with suspected endometriosis, including terms, definitions and measurements: a consensus opinion from the International Deep Endometriosis Analysis (IDEA) group. *Ultrasound Obstet Gynecol* 2016; **48**: 318–332.
19. Van Holsbeke C, Van Calster B, Guerriero S, Savelli L, Paladini D, Lissoni AA, Czekierdowski A, Fischerova D, Zhang J, Mestdagh G, Testa AC, Bourne T, Valentin L, Timmerman D. Endometriomas: their ultrasound characteristics. *Ultrasound Obstet Gynecol* 2010; **35**: 730–740.
20. Okaro E, Valentin L. The role of ultrasound in the management of women with acute and chronic pelvic pain. *Best Pract Res Clin Obstet Gynaecol* 2004; **18**: 105–123.
21. Savelli L, de Laco P, Ghi T, Bovicelli L, Rosati F, Cacciatore B. Tranvaginal sonographic appearance of peritoneal pseudocysts. *Ultrasound Obstet Gynecol* 2004; **23**: 284–288.
22. Van den Bosch T, de Bruijn AM, de Leeuw RA, Dueholm M, Exacoustos C, Valentin L, Bourne T, Timmerman D, Huirne JAF. Sonographic classification and reporting system for diagnosing adenomyosis. *Ultrasound Obstet Gynecol* 2019; **53**: 576–582.
23. Harmsen MJ, Van den Bosch T, de Leeuw RA, Dueholm M, Exacoustos C, Valentin L, Hehenkamp WJK, Groenman F, De Bruyn C, Rasmussen C, Lazzeri L, Jokubkiene L, Jurkovic D, Naftalin J, Tellum T, Bourne T, Timmerman D, Huirne JAF. Consensus on revised definitions of Morphological Uterus Sonographic Assessment (MUSA) features of adenomyosis: results of modified Delphi procedure. *Ultrasound Obstet Gynecol* 2022; **60**: 118–131.
24. Leone FP, Timmerman D, Bourne T, Valentin L, Epstein E, Goldstein SR, Marret H, Parsons AK, Gull B, Istre O, Sepulveda W, Ferrazzi E, Van den Bosch T. Terms, definitions and measurements to describe the sonographic features of the endometrium and intrauterine lesions: a consensus opinion from the International Endometrial Tumour Analysis (IETA) group. *Ultrasound Obstet Gynecol* 2010; **35**: 103–112.
25. Wong M, Crnobrnja B, Liberale V, Dharmarajah K, Widschwendter M, Jurkovic D. The natural history of endometrial polyps. *Hum Reprod* 2017; **32**: 340–345.
26. Valentin L, Hagen B, Tingulstad S, Eik-Nes S. Comparison of 'pattern recognition' and logistic regression models for discrimination between benign and malignant palvic masses: a prospective cross validation. *Ultrasound Obstet Gynecol* 2001; **18**: 357–365.
27. Grimbizis GF, Gordts S, Di Spiezo Sardo A, Brucker S, De Angelis C, Gergolet M, Tin-Chiu L, Tanos V, Brölmann H, Gianaroli L, Campo R. The ESHRE/ESGE consensus on the classification of female genital tract congenital anomalies. *Hum Reprod* 2013; **28**: 2032–2044.
28. Acien P, Acien M, Fernandez F, Mayol MJ, Aranda I. The cavitated accessory uterine mass: A Mullerian anomaly in women with an otherwise normal uterus. *Obstet Gynecol* 2010; **116**: 1101–1109.
29. Naftalin J, Bean E, Saridogan E, Barton-Smith P, Arora R, Jurkovic D. Imaging in Gynecological disease (21): Clinical and ultrasound characteristics of accessory cavitated uterine malformations. *Ultrasound Obstet Gynecol* 2020; **57**: 821–828.
30. Kottner J, Audige L, Brorson S, Donner A, Gajewski BJ, Hrobjartsson A. Guidelines for reporting reliability and agreement studies (GRRAS) were proposed. *J Clin Epidemiol* 2011; **64**: 96–106.
31. Balasch J, Creus M, Fabregues F, Carmona F, Ordi J, Martinez-Roman S. Visible and non-visible endometriosis at laparoscopy in fertile and infertile women and in patients with chronic pelvic pain: a prospective study. *Hum Reprod* 1996; **11**: 387–389.
32. Mishra W, Gaddagi RA, Aggarwal R, Choudhary S, Sharma U, Patel U. Prevalence; Characteristics and management of endometriosis among infertile women: A one year retrospective study. *J Clin Diagn Res* 2015; **9**: QC01–03.
33. Mowers E, Lim C, Skinner B, Mahnert N, Kamdar N, Morgan D. Prevalence of endometriosis during abdominal or laparoscopic hysterectomy for chronic pelvic pain. *Obstet Gynecol* 2016; **127**: 1045–1053.
34. Janssen EB, Rijkers AC, Hoppenbrouwers K, Meuleman C, D'Hooghe TM. Prevalence of endometriosis diagnosed by laparoscopy in adolescents with dysmenorrhea or chronic pelvic pain: a systematic review. *Hum Reprod* 2013; **19**: 570–582.
35. Guo SW, Wang Y. The prevalence of endometriosis in women with chronic pelvic pain. *Gynecol Obstet Invest* 2006; **62**: 121–130.
36. Fuentes A, Escalona J, Cespedes P, Espinoza A, Johnson MC. Prevalence of endometriosis in 287 women undergoing surgical sterilisation in Santiago, Chile. *Rev Med Chile* 2014; **142**: 16–19.
37. Tissot M, Audebert A. Clinical presentation of endometriosis identified at interval laparoscopic tubal sterilization: Prospective series of 465 cases. *J Gynecol Obstet Hum Reprod* 2017; **46**: 647–650.

38. Rawson JM. Prevalence of endometriosis in asymptomatic women. *J Reprod Med* 1991; **36**: 513–515.

39. Chu KK, Chen FP, Chang SD. Prevalence of women undergoing laparoscopic procedures. *Diag Ther Endosc* 1995; **2**: 35–37.

40. Guo S, Wang Y. Sources of heterogeneities in estimating the prevalence of endometriosis in infertile and previously fertile women. *Fertil Steril* 2006; **86**: 1584–1595.

41. Sarria-Santamaria A, Orazumbekova B, Terzic M, Issanov A, Chaowen C, Asunsolo-del-Barco A. Systematic Review and Meta-Analysis of Incidence and Prevalence of Endometriosis. *Healthcare (Basel)* 2020; **9**: 29.

42. Peterson CM, Johnstone EB, Hammoud AO, Stanford JB, Varner MW, Kennedy A, Chen Z, Sun L, Fujimoto VY, Hediger ML, Buck Louis GM; ENDO Study Working Group. Risk factors associated with endometriosis: importance of study population for characterizing disease in the ENDO study. *Am J Obstet Gynecol* 2013; **208**: 451.e1–11.

43. Andolf E, Thorsell M, Kallen K. Caesarean section and risk for endometriosis: a prospective cohort study of Swedish registries. *BJOG* 2013; **120**: 1061–1065.

44. Liu X, Long Q, Guo S. Surgical history and the risk of endometriosis: a hospital-based case–control study. *Reprod Sci* 2016 ; **23**: 1217–1224.

45. Bafort C, Beebeejaun Y, Tomassetti C, Bosteels J, Duffy JM. Laparoscopic surgery for endometriosis. *Cochrane Database Syst Rev* 2020; **10**: CD011031.

46. Tanbo T, Fedorcsak P. Endometriosis-associated infertility: aspects of pathophysiological mechanisms and treatment options. *Acta Obstet Gynecol Scand* 2017; **96**: 659–667.

47. Bean E, Cutner A, Saridogan E, Wong M, Naftalin J, Jurkovic D. Hemoperitoneum as a precursor of deep pelvic endometriosis: prospective cohort study. *Ultrasound Obstet Gynecol* 2019; **54**: 389–394.

48. Bricou A, Batt RE, Chapron C. Peritoneal fluid flow influences anatomical distribution of endometriotic lesions: why Sampson seems to be right. *Eur J Obstet Gynecol Reprod Biol* 2008; **138**: 127–134.

49. Piriyev E, Schiermeier S, Romer T. Coexistence of endometriomas with extraovarian endometriosis and adhesions. *Eur J Obstet Gynecol* 2021; **263**: 20–24.

50. Exacoustos C, De Felice G, Pizzo A, Morosetti G, Lazzeri L, Centini G, Piccione E, Zupi E. Isolated ovarian endometrioma: a history between myth and reality. *J Minim Invasive Gynecol* 2018; **25**: 884–891.

51. Working group of ESGE, ESHRE and WES,Keckstein J, Becker CM, Canis M, Feki A, Grimbizis G, Hummelshoj L, Nisolle M, Roman H, Saridogan E, Tanos V, Tomassetti C, Ulrich UA, Vermeulen N, De Wilde RL. Recommendations for the surgical treatment of endometriosis. Part 2: deep endometriosis. *Hum Reprod Open* 2020; **2020**: hoaa002.

52. Di Donato N, Montanari G, Benefenati A, Leonardi D, Bertoldo V, Monti G, Raimondo D, Seracchioli R. Prevalence of adenomyosis in women undergoing surgery for adenomyosis. *Eur J Obstet Gynecol Reprod Biol* 2014; **181**: 289–293.

53. Eisenberg VH, Arbib N, Schiff E, Goldenberg M, Seidman DS, Soriano D. Sonographic signs of adenomyosis are prevalent in women undergoing surgery for endometriosis and may suggest a higher risk of infertility. *Biomed Res Int* 2017; **2017**: 8967803.

54. Lazzeri L, Di Giovanni A, Exacoustos C, Tosti C, Pinzauti S, Malzoni M, Petraglia F, Zupi E. Prepoerative and postoperative clinical and transvaginal ultrasound findings of adenomyosis in patients with deep infiltrating endometriosis. *Reprod Sci* 2014; **21**: 1027–1033.

55. Kunz G, Beil D, Huppert P, Noe M, Kissler S, Leyendecker G. Adenomyosis in endometriosis: prevalence and impact on fertility. Evidence from magnetic resonance imaging. *Hum Reprod* 2005; **20**: 2309–2316.

56. Leyendecker G, Bilgicyildirim A, Inacker M, Stalf T, Huppert P, Mall G, Böttcher B, Wildt L. Adenomyosis and endometriosis. Re-visiting their association and further insights into the mechanisms of auto-traumatisation. An MRI study. *Arch Gynecol Obstet* 2015; **291**: 917–932.

57. Bergholt T, Erikson L, Berendt N, Jacobsen M, Hertz JB. Prevalence and risk factors of adenomyosis at hysterectomy. *Hum Reprod* 2001; **16**: 2418–2421.

58. Horne AW, Daniels J, Hummelshoj L, Cox E, Coopr KG. Surgical removal of superficial peritoneal endometriosis for managing women with chronic pelvic pain: time for a rethink? *BJOG* 2019; **126**: 1414–1416.