An ultrasound study of the prevalence of endometriosis in women attending for early pregnancy assessment: a prospective observational study

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Abstract

Objective To assess the prevalence of endometriosis using pelvic ultrasound examination in women attending for early pregnancy care Design Prospective observational study. Setting A dedicated early pregnancy unit. Population We included 1341 consecutive women who attended for an early pregnancy assessment and had transvaginal ultrasound scans performed by a single clinician. Methods In addition to the presence of endometriosis on ultrasound scan, we collected data on patient demographics and concurrent gynaecological conditions. Data analysis was performed using logistic regression and multivariate analysis. Main outcome measures The prevalence of endometriosis in addition to possible associations with demographic and clinical variables. Results The prevalence of endometriosis in women attending the early pregnancy unit was 4.9% (95% CI 3.8 – 6.2); In 33/66 (50%, 95% CI 37.9 – 62.1) women with endometriosis, this was a new diagnosis made for the first time during their early pregnancy scan. The presence of endometriosis was strongly associated with congenital uterine anomalies (p < 0.001; OR 5.69, 95% CI 2.17 – 14.9) and uterine fibroids (p = 0.004; OR 2.37, 95% CI 1.31, 4.28). Conclusions Endometriosis is present in nearly 5% of women attending for early pregnancy assessment. In half of the women with endometriosis, the diagnosis was made for the first time during pregnancy. We propose that ultrasound may be a useful tool for the detection of endometriosis and to identify pregnant women who may benefit from specialist antenatal care. Funding No funding was obtained for this work. Keywords Endometriosis, Prevalence, Pregnancy, Ultrasonography

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Running title: Prevalence of endometriosis in pregnancy

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Conclusions

Endometriosis is present in nearly 5% of women attending for early pregnancy assessment. In half of the women with endometriosis, the diagnosis was made for the first time during pregnancy. We propose that ultrasound may be a useful tool for the detection of endometriosis and to identify pregnant women who may benefit from specialist antenatal care.

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Tweetable abstract (110 characters):

Almost 5% of pregnant women have ovarian/deep endometriosis and half of these women are unaware that they have this condition.

Introduction

Endometriosis is an oestrogen-dependent chronic inflammatory condition, characterised by the presence of endometrial-like tissue outside of the uterus.[1] Three subtypes of endometriosis are described: superficial peritoneal, ovarian (endometrioma), and deep (infiltrating).[2] The true prevalence of endometriosis is unknown. It is estimated to affect between 6–10% of women of reproductive age[3] and is present in 50% of women with infertility who have evidence of normal ovulation and normospermic partners.[4] In 50-60% of women, endometriosis is associated with debilitating pelvic pain which can have an adverse effect on quality of life.[5] However, a proportion of women are relatively asymptomatic and less likely to attend for diagnostic tests or seek treatment.

The gold standard for diagnosis of endometriosis is histological examination of lesions excised during surgery.[6]However, when surgery is used to detect endometriosis, long delays of up to 7-8 years after onset of symptoms have been reported.[7] There are no accurate non-invasive biomarkers for endometriosis and ultrasound or MRI are the only diagnostic tests which could be used as alternatives to surgery. Following recent advancements in technology and training, ultrasound is widely acknowledged as the first line investigation of choice in women with suspected endometriosis.[8,9] A standardised approach for ultrasound assessment is well described in a recent consensus statement.[10] Transvaginal ultrasound has been shown to have good concordance with laparoscopy for the diagnosis of deep endometriosis (kappa 0.76) and is highly reproducible for the detection of endometriotic cysts and nodules.[11,12]However, ultrasound is not a sensitive tool for the diagnosis of superficial endometriosis.[11]

Naftalin et al. found evidence of ovarian and/or deep endometriosis on transvaginal ultrasound examination in 6.4% of women attending a general gynaecology clinic.[13] There have been no studies on the prevalence of ovarian endometriomas and deep endometriosis in pregnancy and there is no consensus regarding specialist care for women with endometriosis in pregnancy. Recent literature suggests that women with endometriosis have a higher risk of spontaneous miscarriage, preterm birth, small for gestational age babies, placenta praevia, antepartum haemorrhage, postpartum haemorrhage and preterm birth.[14,15] Exacoustos et al reported that women with deep endometriosis have increased rates of Caesarean sections and surgical complications.[16] Imaging offers the potential to diagnose endometriosis in early pregnancy and identify women at higher risk of adverse pregnancy outcomes.

The aim of this study was to assess the prevalence of ovarian endometriomas and deep endometriosis in women attending a dedicated early pregnancy assessment unit.

Methods

This was a prospective observational study of women attending the Early Pregnancy Assessment Unit at University College London Hospital between April 2017 and March 2019. Only clinically stable women who presented with mild to moderate vaginal bleeding and/or pelvic pain were included into the study. They were all seen by a single operator (E.B) who had extensive experience in scanning of women with endometriosis in a tertiary Endometriosis Centre. A single operator was used in order to reduce the inter-observer variability associated with ultrasound diagnosis of endometriosis. We recorded women's demographic data, indications for attendance and a detailed medical history. This included their age, ethnicity, body mass index (kg/m^2), smoking status, gravidity and parity. All pregnant women that had a transvaginal ultrasound scan were included in the study. All scans were performed in a standard fashion using a 7.5-Mhz probe (Voluson E8, GE Medical Systems, Milwaukee, WI, USA). The uterus was examined for the presence of congenital uterine anomalies, adenomyosis and fibroids. Congenital uterine anomalies were described using the revised ASRM classification.[17] The diagnosis of adenomyosis and fibroids was made in accordance with previously described diagnostic criteria.[13,18] The ovaries and adnexae were then examined. Women were considered to have a diagnosis of endometriosis if there was evidence of endometriotic ovarian cysts and/or deep endometriotic nodules. Ovarian endometriomas were defined as thick-walled and well circumscribed cysts with low-level internal echoes ('ground glass').[19] Endometriotic nodules present as hypoechoic or isoechogenic solid lesions with irregular borders that were fixed to surrounding pelvic structures.[10,20]Statistical analysis was performed

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to establish the prevalence of endometriosis in addition to possible associations between demographic and clinical variables using logistic regression and multivariate analysis. Analysis was performed using SPSS software (SPSS Inc., Chicago, IL, USA). All clinical findings were stored in a clinical database that facilitated data entry and retrieval (PIA-Fetal Database, Viewpoint Bildverabeitung GmbH, Wessling, Germany). The study was registered on Research Registry (Unique identifying number: researchregistry4569). A retrospective audit of records of 750 women who attended our unit during the first trimester of pregnancy (4-14 weeks' gestation), showed a 3.2% prevalence of ovarian and deep endometriosis. Based on this information we calculated that the required sample size for our study was 1176 to achieve a precision of 1% with 95% confidence interval.

Results

During the two-year study period, 1442 consecutive women with suspected early pregnancy complications attended the Early Pregnancy Assessment Unit for a total 1711 ultrasound scans that were all carried out by a single clinician. When women presented for more than one pregnancy during the study period, only findings from the first pregnancy were included in the data collection. Of the 1442 women, 101 (7.0%, 95% CI 5.7 – 8.3) were excluded from the data analysis as they did not undergo a transvaginal ultrasound scan. The median age of the 1341 women included in the final data analysis was 33 years (range 16 – 51), the median parity was 0 (range 0 - 9) and the median BMI was 23.3 (range 15.8 – 56.2). 1233/1341 (91.9%, 95% CI 90.5 – 93.4) women conceived spontaneously and the remaining 108 women conceived after fertility treatment. There were 72 women with a previous diagnosis of endometriosis, 44 of whom had undergone surgical excision of the disease. The indications for attendance at the Early Pregnancy Clinic are provided in the supplementary material (Table S1).

Evidence of ovarian endometriomas and/or deep endometriosis was found in a total of 66/1341 (4.9%, 95% CI 3.8 – 6.2) women. Demographic characteristics of women with and without ultrasound evidence of endometriosis are shown in Table 1. We found ovarian endometriomas in 9/66 (13.6%, 95% CI 5.3 – 21.9) women, 33/66 (50.0%, 95% CI 37.9 - 62.1) had deep endometriosis and 24/66 (36.4%, 95% CI 24.8 – 48.0) had evidence of both ovarian and deep endometriosis. In women with ovarian endometrioma, 26 cysts were identified in the right ovary and 22 in the left ovary. In the 57 women with endometriotic nodules, the most common site was the rectovaginal space (n = 50) and in the region of the uterosacral ligaments (n = 37). The median number of nodules was 2 (range 0 - 7). Bowel involvement was diagnosed in 17/57 (29.8%, 95% CI 17.9 – 41.7) women with deep endometriosis and 2/57 (3.5%, 95% CI 0 – 8.3) had evidence of bladder/vesicouterine involvement.

For 33/66 (50%, 95% CI 37.9 – 62.1) women with evidence of endometriosis, this was a new diagnosis made for the first time during their early pregnancy scan. The remaining 33 women were aware of the diagnosis prior to their pregnancy. A further 39/1341 (2.9%, 95% CI 2.0 – 3.8) women reported a previous diagnosis of endometriosis, of which 32/39 (82.1, 95% CI 70.1 – 94.1) had undergone surgical treatment. However, none of these 39 women had evidence of active endometriotic lesions on ultrasound at the time of their attendance to the early pregnancy unit.

The proportion of women with endometriosis who conceived after fertility treatment (21.2%, 95% CI 12.1-33.0) was much higher compared to women without endometriosis (7.5%, 95% CI 6.1-9.0). A total 8/33 (24.2%, 95% CI 9.6 – 38.8) of women with known endometriosis conceived following fertility treatment which was similar to 6/33 (18.2%, 95% CI 5.0 – 31.4) women with a new diagnosis (p = 0.5540).

The list of all gynaecological diagnoses following pelvic ultrasound examination are documented in Table 2. In 33/66 (50%, 95% CI 37.4 – 62.6) women with evidence of endometriosis, endometriosis was an isolated abnormality. In the remaining 33 women, concomitant abnormalities were also noted on pelvic ultrasound examination (Table 3).

The results of a univariate analysis suggested that the presence of endometriosis was significantly associated with infertility, low parity, congenital uterine anomalies, fibroids and adenomyosis. The largest effect was for congenital uterine anomalies, where the odds of concurrent endometriosis was five times higher than in

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women without. There was also some difference between ethnicities. The results of the univariate analysis are included in the supplementary material (Table S2). The results of a multivariate analysis examining these associations is shown in Table 4. The analysis suggested that ethnicity, infertility, congenital uterine anomalies and fibroids were associated with the presence of endometriosis. After adjusting for these variables, there was no further evidence that either parity or adenomyosis were associated with the presence of endometriosis. East Asian women had the highest chance of endometriosis, with odds over 50% higher than for Caucasian women. Women that conceived following fertility treatment had a higher endometriosis risk, with the odds being over three times higher than those who did not undergo fertility treatment. The presence of congenital uterine anomalies remained strongly associated with the presence of endometriosis.

Discussion

Main findings

In our study, we have demonstrated that the prevalence of ovarian and deep endometriosis in women who attended for early pregnancy assessment was nearly 5%. East Asian ethnicity, infertility, congenital uterine anomalies and fibroids were all associated with the presence of endometriosis on multivariate analysis.

Strengths and limitations

The majority of previous studies that have estimated the prevalence of endometriosis were focused on women who were symptomatic of pelvic pain or were undergoing fertility tests. Our study is the first to describe the prevalence of endometriosis in women during pregnancy, regardless of their previous gynaecological history. We found that the prevalence of endometriosis in women attending our early pregnancy unit (5%) was similar to that in women attending our general gynaecological diagnostic clinic (6%).[13]

The main strength of our study is that it is a large prospective study with clearly defined diagnostic criteria. All examinations were performed by a single operator to avoid inter-observer variability. Consecutive women were screened using a consistent approach to ultrasound examination technique and the same high-quality ultrasound technology. Consistent data collection was ensured and included multiple demographic and clinical variables in order to examine possible associations with the presence of endometriosis.

A possible limitation of our study is the lack of surgical or histological confirmation of the diagnosis of endometriosis. However, the diagnostic criteria were clearly defined in the study methodology and expert ultrasound examination has been well-described in the literature as having good concordance with laparoscopy for the detection of moderate and severe endometriosis.[11] In addition, superficial peritoneal disease cannot be reliably detected on transvaginal ultrasound and therefore the true prevalence of endometriosis is likely to be higher than found in our study. However, the clinical significance of superficial peritoneal endometriosis has been recently questioned and its relevance in the context of adverse pregnancy outcomes is unlikely to be comparable to that of ovarian and deep disease.[21] We were unable to detect deep or ovarian endometriosis in some women who reported past diagnosis of endometriosis. However, the subtype of their previous diagnosis was not known and more than 80% had previously undergone surgical treatment.

Interpretation

In this population, approximately half of women with endometriosis were asymptomatic of endometriosis and were diagnosed for the first time in pregnancy. This is in agreement with previous studies which showed that endometriosis is a relatively common finding in asymptomatic, fertile women.[22] In our study population, women with endometriosis were more likely to have conceived using assisted reproductive techniques. The proportion of women with a new diagnosis of endometriosis that conceived following fertility treatment was similar to that of women with known endometriosis. These findings support the theory that women with difficulty conceiving or undergoing fertility treatment are likely to have a higher prevalence of pelvic endometriosis.[4,23] In our study, the proportion of pregnancies conceived following fertility treatment was high, which is likely to reflect the high number of IVF treatment cycles performed in the local central urban area.

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Our study demonstrated that only 14% of women with ultrasound features of endometriosis had evidence of endometrioma in the absence of deep nodules. These findings support those of Exacoustos et al (2018) that reported ovarian endometriomas as rarely isolated lesions, but commonly associated with pouch of Douglas obliteration, pelvic adhesions and the presence of endometriotic nodules.[24] Our study showed that 15% of women of East Asian origin had evidence of pelvic endometriosis. This supports previous findings that moderate-to-severe endometriosis is more common in women with East or South East Asian ethnicity attending a tertiary referral centre.[25]

The relationship between adenomyosis and endometriosis has previously been described in the literature. Naftalin et al (2012) found that women with a previous or current diagnosis of endometriosis were significantly more likely to have adenomyosis, with an odds ratio of 4.06 (95% CI: 2.25–7.33).[13] Di Donato et al (2014) demonstrated a 21.8% prevalence of adenomyosis in women affected by endometriosis.[26] In our study of pregnant women with endometriosis we did not find as strong an association with adenomyosis as previously reported. However, women in our study population were much younger (median age 33 vs 40 in the study by Naftalin et al.)[13] which could explain our finding of much lower prevalence of adenomyosis in women with and without endometriosis.

Conclusion

Our study has demonstrated the prevalence of ovarian and deep endometriosis on ultrasound scans in women attending for early pregnancy assessment. Half of the women with evidence of endometriosis were asymptomatic and the diagnosis was made for the first time during pregnancy. In view of our findings, we propose that ultrasound may be a useful tool for the detection of endometriosis and to identify pregnant women who may benefit from specialist antenatal care. Further work is needed to determine whether women with a new first trimester ultrasound diagnosis of deep endometriosis are also at increased risk of adverse pregnancy outcomes.

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Disclosure of interests

All authors declare no conflicts of interest.

Contribution to authorship

EB designed the study, coordinated data preparation, analysed and interpreted the data, drafted and revised the manuscript and approved the final manuscript as submitted.

JN supervised data collection, critically reviewed the manuscript and approved the final manuscript as submitted.

AH aided in the design of the study, interpretation of the results, critically reviewed the manuscript and approved the final manuscript as submitted.

ES aided in the design of the study, critically reviewed the manuscript and approved the final manuscript as submitted.

AC aided in the design of the study, critically reviewed the manuscript and approved the final manuscript as submitted.

DJ designed, conceptualised and supervised the study, participated in analyses and interpretation of data, revised the manuscript and approved the final manuscript as submitted.

Details of ethical approval

Ethical approval was sought and approved by the West Midlands – Coventry & Warwickshire Research Ethics Committee (Date of approval: 26th September 2017, reference: 17/WM/0315).

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