Can ultrasound reliably assess ovarian endometriomas in pregnancy? A systematic review

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ABSTRACT

Background and purpose: There is currently a lack of evidence regarding the diagnostic accuracy of ultrasound in assessing endometriomas in pregnancy. The purpose of this study was to systematically review the current evidence reporting on the diagnostic accuracy of ultrasound in assessing endometriomas in pregnancy.

Methods: The Cochrane Register of Controlled Trials, PubMed and EMBASE databases were searched. All types of clinical studies that utilised ultrasound for the diagnosis of ovarian endometriomas in pregnancy were screened. Only studies that obtained histological confirmation were included. The quality of each study was assessed for risk of bias. The diagnostic performance of ultrasound in each of the study types was calculated, and 2x2 contingency tables were constructed to assess the pooled diagnostic performance of ultrasound in assessing endometriomas in pregnancy.

Results: The initial search yielded 4913 papers, of which 1873 qualified for abstract screening. In total, 17 papers were included which consisted of 1 prospective observational study, 3 retrospective observational studies, 4 case series and 9 case reports. There was a combined adnexal mass count of 207, with histology available for 71 (34%). The mean gestational age at the time of ultrasound diagnosis was 12.150 weeks (95% CI: 6.931-17.369). The mean patient age was 33.750 years (95% CI: 30.738-36.762). In 14 of the 17 studies the modality of ultrasound used was stated: transvaginal in 6/14 (43%) transabdominal in 3/14 (21%), and a combination of the two in 5/14 (36%). The quality assessment scores ranged from 50-100% (mean 73%). The International Ovarian Tumor Analysis (IOTA) Simple Rules were used in 2 studies, while subjective impression was used in 14/17. Overall pooled sensitivity, specificity, positive likelihood ratio (LR+), and negative likelihood ratio (LR–) of ultrasound for detecting endometriomas in pregnancy were 0.77 (95% CI: 0.41-0.95), 0.67 (95% CI: 0.16-0.96), 0.33, and 0.34, respectively.

Conclusion: There is currently a lack of high-quality prospective studies to guide the clinician on how to diagnose and manage ovarian endometriomas in pregnancy. The accuracy of ultrasound in deciphering benign endometriomas from malignant masses appears to be less in pregnant than in non-pregnant women. Further work is required to assess the role of ultrasound models for assessing endometriomas in pregnancy.

KEYWORDS

Endometriosis, endometrioma, pregnancy, ultrasound, diagnostic.

Introduction

Routine antenatal care involves the use of ultrasound to assess fetal wellbeing [1]. While the National Health Service Fetal Anomaly Screening Programme does not mandate assessment of the adnexa, many ultrasound practitioners routinely perform this assessment [2]. Adnexal masses in pregnancy are common, with a quoted incidence of 0.19 to 8.8% [3]. Detection rates are increasing which is likely due to growing availability and improving quality of ultrasound systems [4]. Endometriomas account for 4-5% of all adnexal masses diagnosed in pregnancy [5]. In the non-pregnant state endometriomas can be diagnosed with an accuracy of 92% [6]. However, pregnancy poses challenges to the ultrasound practitioner. The expanding uterus limits the use of the transvaginal approach, and adaptations in ovarian vascular tone may alter Doppler findings [7]. Altered progesterone concentrations lead to a phenomenon known as 'decidualisation', which is metaplasia of the sub-coelomic pluripotent mesenchymal cells; decidualisation induces temporary structural and vascular changes that may mimic malignancy on ultrasound [8]. Additionally, ultrasound tools that improve the diagnostic accuracy such as the International Ovarian Tumour Analysis (IOTA) Simple Rules have not been ratified in pregnancy [9].

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Malignancy in this cohort is rare [3]. Surgery during pregnancy is associated with adverse maternal and fetal outcomes, meaning conservative management should be the default [10]. Where possible, surgery should be delayed until the second trimester in order to minimise the risk of miscarriage due to damage to the corpus luteum and loss of luteal support [11]. In the non-pregnant state MRI can be a useful adjunct to ultrasound for assessing adnexal masses [12]. However, interpreting MRI in pregnancy requires subspecialist skills and experience; moreover, image quality is reduced since gadolinium is contraindicated and also because of fetal movement artefacts [13]. As ultrasound is cheaper and more readily available, it is the imaging modality of choice, however, evidence is lacking on its reliability in pregnancy. The objective of this study was to systematically review the current evidence reporting on the diagnostic performance of ultrasound in assessing suspected endometriomas. Secondary objectives were to review what, if any, ultrasound tools or models are being used to assess such masses and, when MRI is utilised, the agreement rate between it and ultrasound. An appreciation of the accuracy of ultrasound in assessing these challenging masses in pregnancy will hopefully serve to reduce unnecessary patient and clinician anxiety and unneeded interventions.

Methods

Search Strategy

PubMed, EMBASE and The Cochrane Register of Controlled Trials were searched from January 2000 to January 2021. Titles, abstracts and MESH terms were searched for all combinations of words for adnexa (ovary, ovarian, fallopian tube, tubal, broad ligament, parametrial, parametrium); adnexal mass (cyst, tumour, neoplasm, malignancy, borderline tumour, adenoma, dermoid, teratoma, corpus luteum, corpora, endometrioma); imaging (ultrasound, transvaginal, transabdominal, computer tomography, CT, magnetic resonance imaging, MRI, MR), and pregnancy (pregnant, gravid, antenatal, gestational). This electronic search strategy is shown in Appendix 1. All included studies were cross-referenced to identify articles not captured by our search.

Inclusion criteria

All Studies, of any type, that identified adnexal masses in pregnancy and used histopathological diagnosis as an outcome measure were included. Only full papers published in English in peer-reviewed journals were assessed. Given the limited number of randomised control trials and large cohort studies, no additional methodological filters were applied. Studies were selected in a two-stage process by two of the authors (JG & ON). First, eligibility was assessed based on the title and abstract, and then the full manuscript was examined to decide on inclusion suitability. If there was disagreement, the third author (AS) was consulted for the final decision.

Data extraction

Data extraction was performed by one author (JG). The following information was recorded (where available): patient age, patient ethnicity, gestational age at diagnosis, presence/absence of symptoms, whether ultrasound performed was transvaginal or transabdominal and the ultrasound assessment tools used (e.g., pattern recognition or IOTA Simple Rules), and whether histopathology was in keeping with the ultrasound diagnosis. The utilisation of MRI and its findings were also recorded as appropriate.

Presentation and quality assessment of data

The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement was used for reporting the methods, results and discussion sections of this review [14]. The STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement was used to assess the quality of prospective and retrospective cohort studies, while the Joanna Briggs Institute (JBI) checklist was used for case reports and case series [15,16]. A total of 34 points can be awarded to studies using the STROBE list, 16 using the JBI checklist for case reports, and 20 using the JBI checklist for case series. This quality assessment was performed independently by two authors (JG & ON) with consultation from the third author (AS) in cases of disagreement. The included papers are listed in tables 1, 2 and 3 in order of quality. The four most relevant outcomes from each checklist are included. The full STROBE and JBI checklists are provided in Appendix 2.

Data analysis

Due to similarities in study design, the case reports and case series are presented collectively, and the prospective and retrospective observational studies are presented together. MedCalc was used to construct 2x2 contingency tables in order to calculate the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy (with 95% confidence intervals) of ultrasound in each study type [17]. The agreement rate between ultrasound and MRI was also calculated. As in a previous review, because of the low estimate weight, case reports and case series were not included in the meta-analysis pooling [18]. Data regarding ultrasound performance were extracted from seven studies. A random-effects model was used to determine pooled sensitivity, specificity, LR+, and LR−. To characterise the clinical utility of a test and to estimate the post-test probability of disease, LR+ and LR− were used. An LR value of 0.2-5.0 was suggested to provide weak evidence for ruling out or confirming the disease; an LR value of 5.0-10.0 or 0.1-0.2 provided moderate evidence, and an LR value of >10 or <0.1 provided strong evidence to either confirm or rule out the disease [19]. Summary receiver-operating characteristics (sROC) curves were plotted to illustrate the relationship between sensitivity and specificity. All analyses were performed using Meta-Analytical Integration of Diagnostic Accuracy Studies (MIDAS) and Meta-Analysis of Diagnostic Accuracy (METANDI) commands in STATA version 14.0 for Windows (Stata Corp., College Station, TX, USA). A p-value of <0.05 was considered statistically significant. One of the limitations to the analysis was that the estimated pooled sensitivity and specificity were not accurate; this issue, which was taken into consideration in the meta-analysis of the data, lies in the fact that two values for the True Positives (TP), True Negatives (TN), False Positives (FP) and False negatives (FN) were zero.

Results

Literature identified

The electronic search of the three databases yielded 4913 papers. Crosschecking of references identified no additional papers. Of the 4913 papers, 1873 qualified for abstract screening. A further 1846 did not meet the inclusion criteria, leaving 27 papers, of which 10 were subsequently excluded for the following reasons: full paper not available in English (4); did not meet eligibility criteria (3); unable to access paper (2); duplicate (1). This is depicted in Figure 1. The final number of papers included in this review was 17: 1 prospective observational study, 3 retrospective observational studies, 4 case series and 9 reports. There was a combined adnexal mass count of 207, however due to incomplete data sets in studies, histology was available for 71 (34%).

Assessment of quality

The quality assessment scores ranged from 50 to 100%. The mean was 79%. These scores, along with four of the most relevant assessment criteria, are shown in Tables 1, 2 and 3 [4,20-35].

Demographics

The studies were undertaken in high, middle, and low-income countries, and in both tertiary referral units and district hospitals. The mean patient age was 33.750 years (95% CI: 30.738-36.762). The vast majority of studies did not state the patient's ethnicity. The mean gestational age at the time of ultrasound diagnosis was 12.150 weeks (95% CI: 6.931-17.369). Patients reported pain in 3/48 (6%) of cases. In 14/17 studies the modality of ultrasound used was stated: transvaginal in 6/14 (43%); a combination of transvaginal and transabdominal in 5/14 (36%), and transabdominal in 3/14 (21%). The prospective study by Zanetta *et al*. was the only study to aim to assess the reliability of ultrasound in diagnosis of adnexal masses in pregnancy [20]. Two studies utilised the IOTA Simple Rules [21,22]. Subjective impression was used in the remaining 15/17. Histology was available for 28 masses assessed using the IOTA Simple Rules.

MRI

MRI was utilised in 11 cases. In all cases it agreed with the ultrasound impression. In 8/11 both ultrasound and MRI incorrectly diagnosed decidualised endometriomas as malignant masses. In the remaining 3/11 both techniques correctly identified decidualised endometriomas. A summary of all study characteristics is given in appendix 3 and 4.

Surgery

Surgery was performed in the antenatal period in 36/71 cases (51%). Timings of surgery were as follows: second trimester

Figure 1 Flow diagram of the literature search.

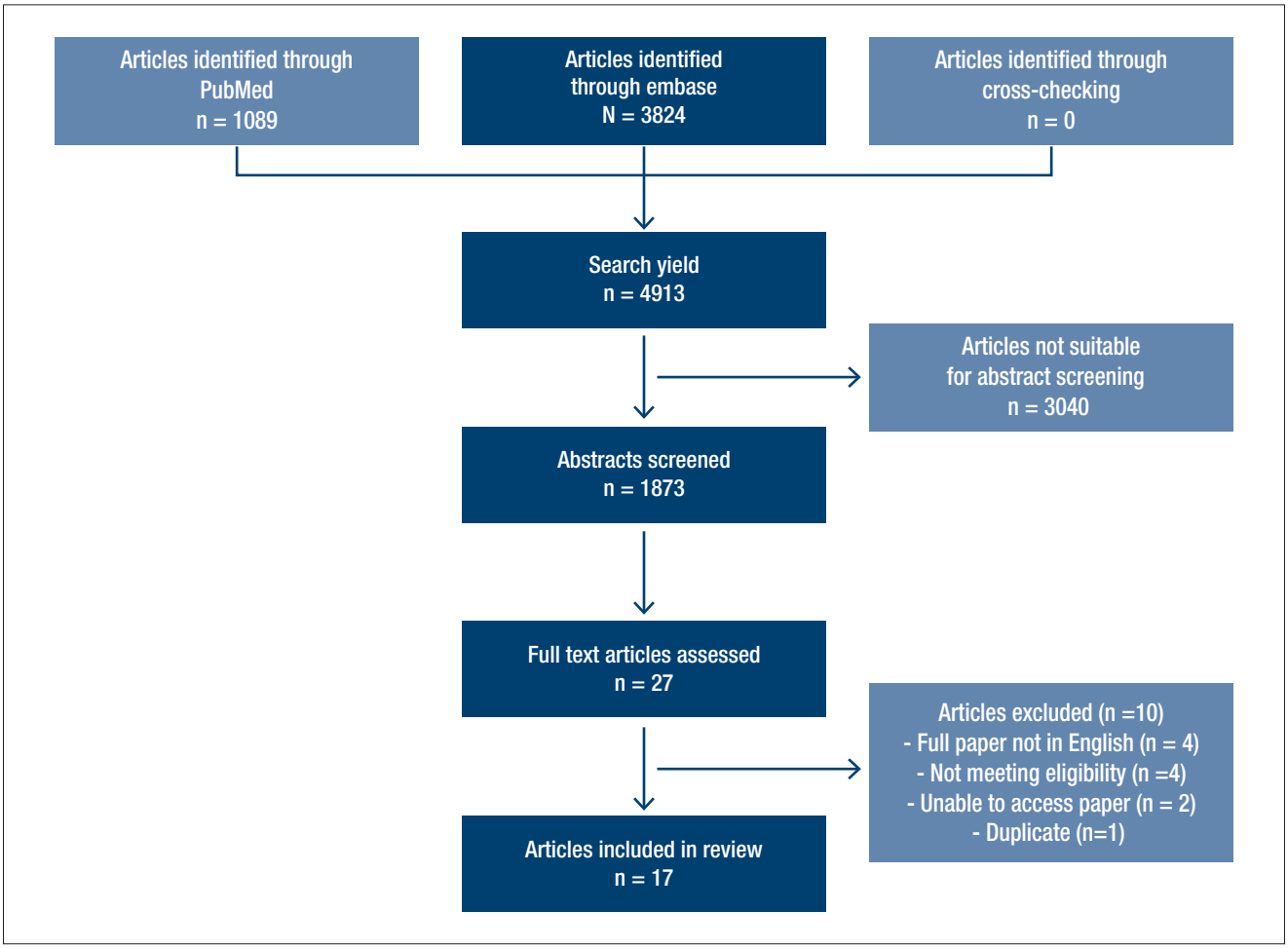


Table 1 Quality assessment of included prospective and retrospective cohort studies performed using the STROBE checklist. The table shows four of the most relevant criteria used and the quality assessment score (%) obtained. Only the first author is listed for each paper (Retro = Retrospective Props = Prospective).

Study	Design	Objectives	Descriptive data	Key results	Interpretation	%
Pateman, 2014 [4]	Retro Cohort	Y	Y	Y	Y	85
Zanetta, 2003 [20]	Prosp Cohort	Y	N	N	Y	63
Bailleux, 2015 [21]	Retro Cohort	Y	Y	Y	Y	80
Mascilini, 2014 [22]	Retro Cohort	Y	Y	Y	Y	77

Table 2 Quality assessment of included case series performed using the Joanna Briggs Institute checklist. The table shows four of the most relevant criteria and the quality assessment score (%) obtained [16]. Only the first author is listed for each paper.

Study	Clear inclusion criteria	Valid method for identification of condition	Standard & reliable method for all participants	Clear clinical information	Outcomes clearly reported	%
Barbieri, 2009 [23]	Y	Y	Y	Y	Y	90
Machida, 2008 [24]	Y	Y	Y	Y	Y	55
Sammour, 2005 [25]	N	Y	Y	Y	Y	55
Yoshida, 2008 [26]	N	Y	Y	Y	Y	55

Table 3 Quality assessment of included case reports performed using the Joanna Briggs Institute. The table shows four of the most relevant criteria and the quality assessment score (%) obtained [16]. Only the first author is listed for each paper.

Study	Clinical history	Diagnostic test	Intervention	Takeaway lessons	%	%
Taylor, 2015 [27]	Y	Y	Y	Y	100	90
Fruscella, 2004 [28]	Y	Y	Y	Y	87	55
Inamdar, 2019 [29]	Y	Y	Y	Y	87	55
Izza Rozalli, 2015 [30]	Y	Y	Y	Y	87	55
Nakai, 2015 [31]	Y	Y	Y	Y	87	90
Sorrentino, 2020 [32]	Y	Y	Y	Y	87	55
Soule, 2020 [33]	Y	Y	Y	Y	87	55
Tazegül, 2013 [34]	Y	Y	Y	Y	87	55
Poder, 2008 [35]	Y	Y	Y	Y	50	55

(33); third trimester (2); first trimester (1). The indication to operate was: suspicion of malignancy (30); severe pain (5); severe pre-eclampsia requiring delivery via caesarean at 32 weeks' gestation with concomitant adnexal surgery (1). Of the 36 surgeries performed, malignancy was detected in 1 patient, and a borderline tumour in 1. Fetal outcome was declared in 34/36 cases: 33/34 pregnancies continued without complication and 1 patient suffered the loss of a 21-week-old fetus 24-hours following surgery. There were no significant maternal complications declared in any of the studies. Adnexal surgery was performed during caesarean section at term in 9 cases. It was unclear in the majority whether there were maternal-fetal indications for section. In 33/36 cases the modality of surgery was documented as: laparotomy (23) and laparoscopy (10).

Pooled results

Only studies with extractable 2 × 2 contingency tables were included in the final meta-analysis. Due to the high risk of bias and their relatively small weight, all case reports and case series were excluded. Overall, the pooled sensitivity, specificity, LR+, and LR– of ultrasound for detecting endometriomas in pregnancy were: 0.77 (95% CI: 0.41-0.95), 0.67 (95% CI: 0.16-0.96), 0.33, and 0.34, respectively. We were unable to construct a Forest plot owing to the number of missing sensitivity or specificity values in some of the studies. Figure 2 illustrates the sROC curve with the summary operating point in relation to the different study estimates.

Discussion

This is the first systematic review to assess the reliability of ultrasound in diagnosing endometriomas in pregnancy. The large database search yield allowed for an extensive review of

the literature and the broad patient and study demographics will allow for generalisability of this review.

A limitation of this review is the poor quality of the available data. The impact of this was controlled as much as possible through the use of validated quality assessment tools and by ranking the studies in score order. In order to facilitate conservative management of adnexal masses in pregnancy, an ultrasound diagnosis is required – be that of the histological subtype, or of benign versus malignant. A number of ultrasound tools have been created to improve the diagnostic accuracy of ultrasound. One of the most widely adopted is the set of IOTA simple descriptors and Simple Rules [36]. Previous studies have shown that these simple rules can be applied to 76% of adnexal masses resulting in a sensitivity of 95%, specificity of 91%, LR+ of 10.37, and a LR– of 0.06 [37]. Only two papers in this review stated that they used IOTA simple rules [21,22]. Due to the fact that these two studies combined have confirmed histology for just 23 masses, it is difficult to draw conclusions on the reliability of simple rules in assessing adnexal masses in pregnancy.

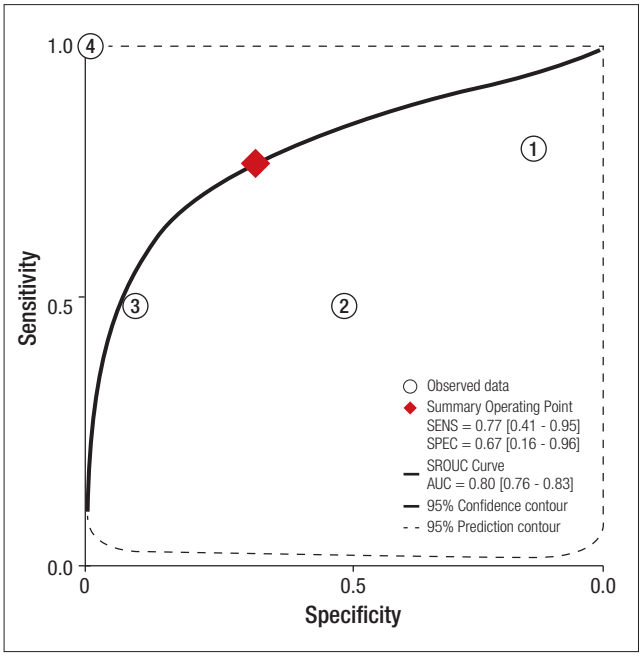
For the remaining studies it is presumed that subjective impression/pattern recognition (PR) was used to reach a diagnosis. No studies stated the experience of the ultrasound practitioners. PR has been shown to be the most accurate means of assessing adnexal masses, with an accuracy rate of 92% [38]. The pooled rate in this review was considerably lower. Reasons for this may be that Timmerman and colleagues' study did not include pregnant women and that it included all histological types of masses [38]. Additionally, Timmerman *et al*. showed that while results were comparable between specialist gynaecologists and sonographers, in less experienced hands the accuracy levels decreased with moderate interobserver agreement [38]. While uncertainty over the level of experience of the ultrasound practitioners may be seen as a limitation, it does increase the generalisability of this review, as most antenatal ultrasounds are performed by practitioners with varying degrees of gynaecological experience.

In cases where an adnexal mass cannot be classified on ultrasound, MRI may prove a useful adjunct despite its aforementioned limitations in pregnancy [39]. The gravid endometrium and decidualised nodules within an endometrioma share striking similarities, and T2 signal intensity and diffusion-weighted imaging can help to exclude malignant transformation [30]. In this review MRI did not prove superior to ultrasound in a single case, and led to incorrect diagnosis of malignancy in 8/11 cases (72%). Although this sample is small, it highlights the need for more research into the reliability of MRI in pregnancy [30].

The over diagnosis of malignancy by both ultrasound and MRI is reflected in the fact that over half of women in this study underwent surgery in the antenatal period. While both growing evidence and this review suggest that surgery is safe in pregnancy, the loss of a potential life following surgery for what transpired to be a benign mass highlights the importance of accurate diagnoses.

This review also highlights that despite the majority of these studies being relatively recent, only 30% of cases were performed laparoscopically. The majority of these cases were performed before 20 weeks and no other reasons were stated

Figure 2 sROC curve for the diagnostic utility of ultrasound in diagnosing endometriomas during pregnancy.



to contraindicate a minimal access approach. While evidence suggests laparoscopy is a safe surgical approach in pregnancy, this most likely reflects a lack of experience amongst health professionals in using it in this setting [40].

In conclusion, this systematic review highlights the challenges posed to the ultrasound practitioner when assessing suspected endometriomas in pregnancy. It also demonstrates the lack of good quality evidence to support the reliability of ultrasound. In cases of uncertainty, MRI may be a useful adjunct, however its reliability in pregnancy is also yet to be established. It should be remembered that malignancy in this cohort is rare, and when suspected expert opinion should be sought before undertaking surgery during the antenatal period. With a current lack of ratified guidelines on the need for, and appropriate timing of assessment of the adnexa in pregnancy, we hope this paper serves to prompt further work towards answering this important question.

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Conflicts of interest: *The authors declare that there are no conflicts of interest.*

Appendices

Appendix 1. Search Strategy for PubMed and EMBASE performed in January 2021

PUBMED		
SEARCH	QUERY	RESULTS
#5	#1 AND #2 AND #3 AND #4	1,089
#4	"pregnant women"[MeSH Terms] OR "pregnancy"[Title/Abstract] OR "pregnant"[Title/Abstract] OR "gravid"[Title/Abstract] OR "antenatal"[Title/Abstract] OR "gestational"[Title/Abstract]	309,769
#3	"adnexa uteri"[MeSH Terms] OR "ovary"[Title/Abstract] OR "ovarian"[Title/Abstract] OR "fallopian tube"[Title/Abstract] OR "tubal"[Title/Abstract] OR "broad ligament"[Title/Abstract] OR "parametrial"[Title/Abstract] OR "parametrium"[Title/Abstract]	154,002
#2	"ultrasonography"[MeSH Terms] OR "imaging"[Title/Abstract] OR "ultrasound"[Title/Abstract] OR "sonography"[Title/Abstract] OR "sonogram"[Title/Abstract] OR "transvaginal"[Title/Abstract] OR "transabdominal"[Title/Abstract] OR "computer tomography"[Title/Abstract] OR "CT"[Title/Abstract] OR "magnetic resonance"[Title/Abstract] OR "MR"[Title/Abstract] OR "MRI"[Title/Abstract]	1,255,107
#1	"ovarian cysts"[MeSH Terms] OR "mass"[Title/Abstract] OR "tumour"[Title/Abstract] OR "tumor"[Title/Abstract] OR "neoplasm"[Title/Abstract] OR "malignancy"[Title/Abstract] OR "borderline"[Title/Abstract] OR "adenoma"[Title/Abstract] OR "dermoid"[Title/Abstract] OR "teratoma"[Title/Abstract] OR "corpus"[Title/Abstract] OR "corpora"[Title/Abstract] OR "endometrioma"[Title/Abstract] OR "cyst"[Title/Abstract]	1,768,737

EMBASE		
SEARCH	QUERY	RESULTS
#5	#1 AND #2 AND #3 AND #4	3824
#4	exp pregnancy/ or pregnancy.mp OR exp pregnant woman OR gravid.mp OR antenatal.mp OR gestational.mp	1, 424, 413
#3	ultrasound.mp. or exp ultrasound OR transvaginal.mp OR transabdominal.mp OR computer assisted tomography.mp. or exp OR CT.mp OR magnetic resonance.mp OR MRI.mp	4, 745, 320
#2	mass.mp. or exp mass OR exp cyst/ or cyst.mp. or exp ovary cyst OR tumour.mp. or exp neoplasm OR malignant.mp OR exp adenoma/ or adenoma.mp OR dermoid.mp. or exp teratoma OR endometrioma.mp OR corpus.mp. or exp corpus luteum	8, 230, 355
#1	exp uterine adnexa OR adnexa*.mp. OR exp ovary OR ovarian.mp. OR fallopian.mp. or exp fallopian tube OR broad ligament.mp. or exp broad ligament OR exp parametrium OR parametrial.mp	697, 802

Appendix 2. Risk of bias assessment tools

A) STROBE CHECKLIST		
DESCRIPTION OF ITEMS		FIRST AUTHOR (YEAR)
1a	Study design is clear in title or abstract	0/1/NA
1b	Abstract provides an informative and balanced summary	
2	Explain the scientific background and rationale for the investigation being reported	
3	State specific objectives, including any prespecified hypotheses	
4	Present key elements of study design early in the paper periods of recruitment, exposure, follow-up, and data collection	
5	Describe the setting, locations, and relevant dates, including	
6a	Give the eligibility criteria and the sources and methods of selection of participants; describe methods of follow-up	
6b	For matched studies, give matching criteria and number of exposed and unexposed	
7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers; give diagnostic criteria, if applicable	
8	For each variable of interest, give data sources and details of methods of assessment	

A) STROBE CHECKLIST	
DESCRIPTION OF ITEMS	**FIRST AUTHOR (YEAR)**
9 Describe any efforts to address potential sources of bias	
10 Explain how the study size was arrived at	
11 Explain how quantitative variables were handled in the analyses; if applicable, describe which groupings were chosen and why	
12a Describe all statistical methods	
12b Describe any methods used to examine subgroups and interactions	
12c Explain how missing data were addressed	
12d Explain how loss to follow-up was addressed	
12e Describe any sensitivity analyses	
13a Report numbers of individuals at each stage of study	
13b Give reasons for non-participation at each stage	
13c Consider use of a flow diagram	
14a Give characteristics of study participants and information on exposures and potential confounders	
14b Indicate number of participants with missing data for each variable of interest	
14c Summarize follow-up time	
15 Report numbers of outcome events or summary measures over time	
16a Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision	
16b Report category boundaries when continuous variables were categorized	
16c If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
17 Report other analyses done	
18 Summarize key results with reference to study objectives	
19 Discuss limitations of the study, taking into account sources of potential bias or imprecision.	
20 Give a cautious overall interpretation of results	
21 Discuss the generalisability of the study results	
22 Give funding sources	
Summary	X/Y (%)

B) JOANNA BRIGGS INSTITUTE CHECKLIST – CASE REPORTS					
Reviewer _____ Date _____					
Author _____ Year _____ Record Number _____					
	YES (2)	**NO (0)**	**UNCLEAR (1)**	**N/A**	**0/1/2**
Were patient's demographic characteristics clearly described?	☐	☐	☐	☐	
Was the patient's history clearly described and presented as a timeline?	☐	☐	☐	☐	
Was the current clinical condition of the patient on presentation clearly described?	☐	☐	☐	☐	

	YES (2)	NO (0)	UNCLEAR (1)	N/A	0/1/2
Were diagnostic tests or assessment methods and the results clearly described?	☐	☐	☐	☐	
Was the intervention(s) or treatment procedure(s) clearly described?	☐	☐	☐	☐	
Was the post-intervention clinical condition clearly described?	☐	☐	☐	☐	
Were adverse events (harms) or unanticipated events identified and described?	☐	☐	☐	☐	
Does the case report provide takeaway lessons?	☐	☐	☐	☐	
Total					X/Y %
Overall appraisal: Include ☐ Exclude ☐ Seek further info ☐					

C) JOANNA BRIGGS INSTITUTE CHECKLIST – CASE SERIES

Reviewer _____ Date _____

Author _____ Year _____ Record Number _____

	YES (2)	NO (0)	UNCLEAR (1)	N/A	0/1/2
Were there clear criteria for inclusion in the case series?	☐	☐	☐	☐	
Was the condition measured in a standard, reliable way for all participants included in the case series?	☐	☐	☐	☐	
Were valid methods used for identification of the condition for all participants included in the case series?	☐	☐	☐	☐	
Did the case series have consecutive inclusion of participants?	☐	☐	☐	☐	
Did the case series have complete inclusion of participants?	☐	☐	☐	☐	
Was there clear reporting of the demographics of the participants in the study?	☐	☐	☐	☐	
Was there clear reporting of clinical information of the participants?	☐	☐	☐	☐	
Were the outcomes or follow up results of cases clearly reported?	☐	☐	☐	☐	
Was there clear reporting of the presenting site(s)/clinic(s) demographic information?	☐	☐	☐	☐	
Was statistical analysis appropriate?	☐	☐	☐	☐	
Total					X/Y %
Overall appraisal: Include ☐ Exclude ☐ Seek further info ☐					

Appendix 3. Table summarising characteristic of prospective & retrospective observational studies.

PAPER	ULTRASOUND DIAGNOSIS (SI)	N	SURGERY	HISTOLOGY	CONSERVATIVE MANAGEMENT	RESOLUTION RATE ON FOLLOW UP SCAN (%)	MRI	IOTA	IOTA INTERPRETATION	TIMING OF SURGERY	INDICATION SURGERY	MATERNAL/ FETAL COMPLICATION
Bailleux et al. 2017.19	Endometrioma	53	10 Cystectomy	4 endometrioma 4 mucinous BOT 1 serous cystadenoma 1 dermoid	43	2 (5%)	0	Y	All benign	2AN 3 C-Section 5 PP	2 risk of torsion 1 torsion, 2 obstetric	No
Zanetta et al 21	Simple Cyst	39	7	5 Serous cystadenoma 2 Functional	32	27/39 (69%)	0	N	-	2 AN 5 PP	2 Torsion	No
	Complex benign	15	3	1 Functional 1 Dermoid 1 Serocele	12	8/15 (57%)	0	N	-	1 AN 2 PP	Torsion	No
	Endometrioma	9	3	1 Serous cystadenoma 1 mucinous cystadenoma 1 endometrioma	7/9 (77%)	0	0	N	-	1 C-Section 2 PP		No
	Dermoid	9	5	5 Dermoid	0 (0%)	0	0	N	-	5 PP		No
	BOT	5	5	3 BOT 2 Dermoid	0	0	0	N	-	5 PP		No
Pateman et al. 2014.4	Endometrioma	36	1	1 endometrioma	35	0	0	-	-	1 C-Section	>	No
Mascilini et al 2014.20	Unclassifiable BOT Malignant	9 8 1	18	18 endometriomas	-	-	0	Y	12: Unclassifiable 1 Malignant 5- Benign	13 AN 5 C-Section	malignant	Not documented
AN = Antenatal, PN = Postnatal, BOT = Borderline Ovarian Tumour)												

Appendix 4. Table summarising results of case reports and case series

ULTRASOUND DIAGNOSIS	N	SURGERY	HISTOLOGY/ CYTOLOGY	CONSERVATIVE MX	RESOLUTION RATE (%)	US ACCURACY	MRI	MRI & US AGREEMENT (%)	MRI SUPERIOR TO US	TIMING OF SURGERY	FETO-MATERNAL COMPLICATIONS
Malignant	13	13	13 Decidualised endometrioma	0	-	0/13 (0%)	9	7/9 (78%)	2 - endometrioma	12 AN 1 C-Section	No
Decidualised Endometrioma	6	5	3 Decidualised endometrioma 1 Serous BOT 1 clear cell cancer	-	1	4/6 (67%)	3	3/3 (100%)	-	3 AN 1 C-Section 1 PP	No
Complex	1	1	1 Decidualised endometrioma	0	-	-	0	-	-	1 AN	No
AN = Antenatal, PN = Postnatal, BOT = Borderline Ovarian Tumour)											