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Ovarian ectopic pregnancy: clinical characteristics, ultrasound diagnosis and management

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KEYWORDS: ectopic pregnancy; ovarian ectopic; ovarian pregnancy; ultrasound

CONTRIBUTION

What are the novel findings of this work?
High-resolution B-mode imaging with color Doppler and ultrasound-guided palpation of pelvic organs increases the sensitivity of preoperative diagnosis of ovarian ectopic pregnancy (OEP). OEP is more likely to contain an embryo and present with severe hemoperitoneum compared with tubal ectopic pregnancy, which should aid the differential diagnosis between these two types of extrauterine ectopic pregnancy.

What are the clinical implications of this work?
Preoperative detection of OEP on ultrasound avoids delay in starting treatment, optimizes surgical management and helps to reduce adverse outcomes, such as the need for blood transfusion and oophorectomy.

ABSTRACT

Objective *To compare the clinical, ultrasound and biochemical characteristics of ovarian ectopic pregnancy (OEP) with those of tubal ectopic pregnancy (TEP).*

Methods *This was a retrospective case–control study of women with OEP and those with TEP seen at a single center between December 2010 and February 2021. OEP was defined as a pregnancy located completely or partially within the ovarian parenchyma, seen separately to a corpus luteum, if a corpus luteum was present within the ipsilateral ovary. We compared demographic features, risk factors, clinical presentation, ultrasound findings and outcomes, such as blood loss at surgery, need for blood transfusion, length of hospital stay, follow-up and future pregnancy outcome, between cases of OEP and TEP.*

Results *Overall, 20 women with OEP were identified and compared to 100 women with TEP. A total of 15/20 (75%) OEPs were diagnosed correctly on the first ultrasound scan. There was no difference between the groups in terms of maternal age, gestational age, gravidity, parity or risk factors. Compared with TEP, OEP was more likely to present with abdominal pain without vaginal bleeding (12/20 (60%)* vs *13/100 (13%); odds ratio (OR), 10.0 (95% CI, 3.45–29.20);* $P < 0.01$*), contain an embryo with cardiac activity (3/20 (15%)* vs *2/100 (2%); OR, 8.7 (95% CI, 1.34–55.65);* $P = 0.02$*) and have severe hemoperitoneum on ultrasound (9/20 (45%)* vs *8/100 (8%); OR, 9.4 (95% CI, 3.01–29.40);* $P < 0.01$*), and had a higher volume of blood loss at surgery (median, 700 mL* vs *100 mL;* $P < 0.01$*). All surgically managed OEPs had successful laparoscopic treatment (18 excisions, one wedge resection) with preservation of the ovary. Only one (5%) case of OEP required a blood transfusion.*

Conclusions *OEP is more likely than TEP to contain an embryo and to present with severe hemoperitoneum. In a dedicated early pregnancy setting, the majority of OEPs were detected on an ultrasound scan at the initial visit, facilitating optimal minimally invasive surgical management, reducing the risk of blood transfusion and oophorectomy. Our findings can be used as a reference for clinicians who may not otherwise encounter this rare condition.* © *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

An ovarian ectopic pregnancy (OEP) is a rare form of ectopic pregnancy that is implanted completely or partially within the ovarian parenchyma[1]. A recent

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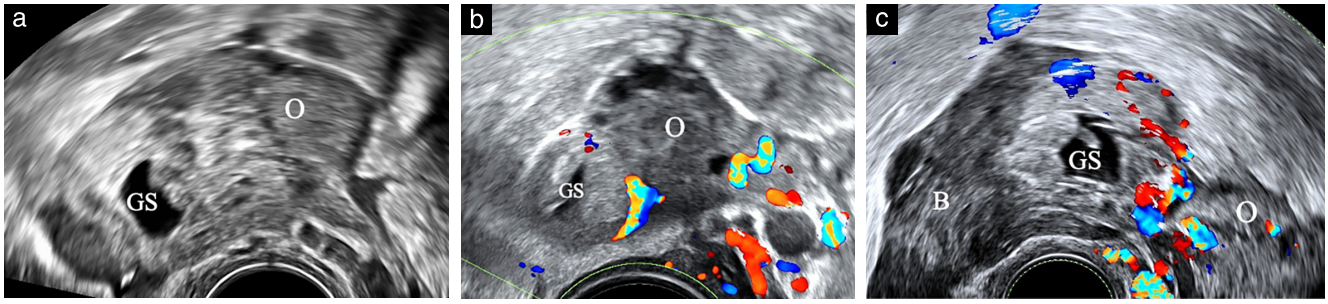

Figure 1 Grayscale (a) and color Doppler (b,c) transvaginal ultrasound images of ovarian ectopic pregnancies, showing: (a) gestational sac (GS) confined within ovary (O); (b) GS with prominent blood supply protruding partially outside O; and (c) GS protruding through O adjacent to blood clots (B).

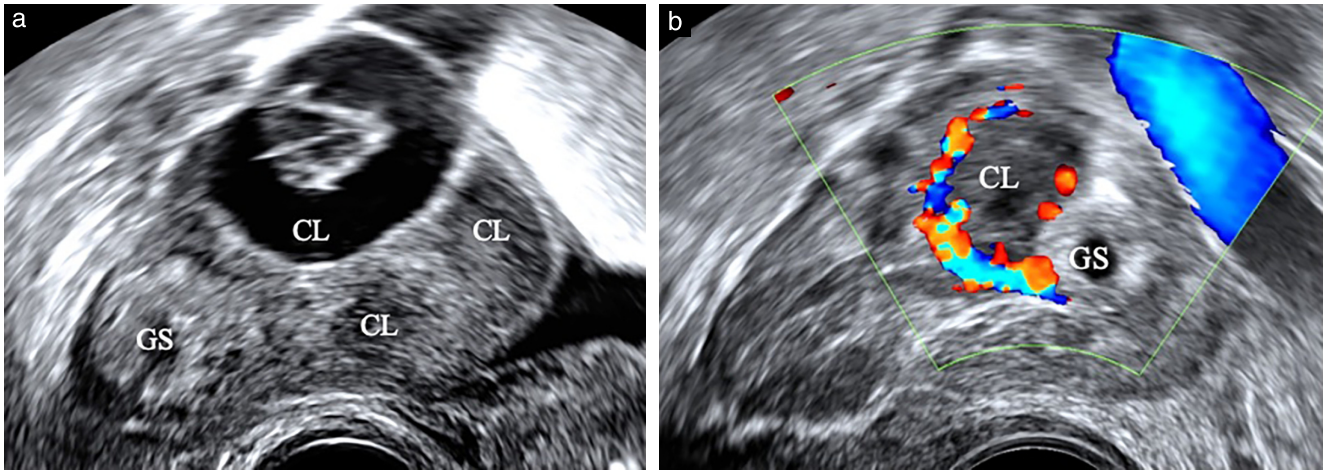

Figure 2 Grayscale (a) and color Doppler (b) transvaginal ultrasound images of ovarian ectopic pregnancies, demonstrating: (a) gestational sac (GS) seen separately to multiple corpora lutea (CL); and (b) vascularity of CL seen separately to GS.

systematic review[2] identified only 82 case reports of OEP in the international literature between 2011 and 2022. Although non-invasive diagnosis of ectopic pregnancy at other sites, such as tubal ectopic pregnancy (TEP) or Cesarean scar pregnancy, has improved in recent years, OEP is still detected mostly at emergency surgery. This could be explained by the relative rarity of OEP and the small number of early pregnancy specialists who have experience with the management of more than a handful of OEPs in their practice. In addition, the differential diagnosis between OEP and TEP can be difficult, and is rarely made on B-mode imaging alone without utilizing color Doppler and palpation of pelvic organs with the ultrasound probe. Some case reports in the literature date back several decades, when resolution of ultrasound machines was lower, which could explain the relatively poor diagnostic accuracy in older studies.

However, an early diagnosis of OEP is important as it is associated with higher maternal morbidity compared to TEP and requires more proactive management. A correct preoperative diagnosis of OEP facilitates better planning or surgery, which is often more complex compared with surgical treatment of TEP and requires a higher level of surgical skill. OEP can be difficult to identify at surgery and, without a correct preoperative diagnosis, is sometimes impossible to differentiate from a corpus luteum (CL). This could lead to a false-negative diagnosis of OEP at laparoscopy or a false-positive diagnosis of TEP, resulting in unnecessary loss of, or injury to, the Fallopian tube.

The aim of this study was to analyze the demographic, clinical, ultrasound and biochemical characteristics recorded in women diagnosed with OEP and compare them to those of a randomly selected group of patients with TEP, in order to identify features which could facilitate a non-invasive diagnosis of OEP and help to improve the differential diagnosis between these two types of extrauterine ectopic pregnancy.

Background

Epidemiology

OEP accounts for 1–3% of ectopic pregnancies and 0.03–0.09% of all pregnancies[3–6]. The reported incidence of OEP appeared to be increasing up to the mid-1990s, but has since remained stable. This is likely due to better diagnosis on imaging and more liberal use of laparoscopy for both the diagnosis and treatment of ectopic pregnancies, which came into effect around 30 years ago[3,7,8].

Macroscopy

Macroscopically, OEP may be confined to the ovarian parenchyma or protrude partially through the ovarian

capsule (Figure 1). It is usually seen separately to a CL, if within the ipsilateral ovary (Figure 2). At surgery or on macroscopic examination, a primary OEP may be difficult to distinguish from a secondary OEP (tubal pregnancy implanting subsequently into the ovary). In 1878, Spiegelberg[9] proposed criteria for the surgicopathological diagnosis of primary ovarian pregnancy. He stated that the Fallopian tubes should be intact and separate from the ovary, the gestational sac should be implanted into the ovary and there should be evidence of ovarian tissue attached to the pregnancy specimen. Although Spiegelberg's criteria are still referred to in recent literature, they are of limited value for modern clinical practice. The health of Fallopian tubes is also of limited relevance, as the finding of tubal abnormalities and adhesions does not necessarily mean that the ectopic pregnancy originated there. In addition, a TEP could be expelled through the fimbrial end of the tube and reimplant into the ovary without causing tubal rupture. The challenge for both ultrasound and surgery is to distinguish an OEP from a CL or a functional hemorrhagic cyst. By using more advanced surgical techniques, most OEPs can be excised from the ovary without removing any ovarian tissue.

Microscopy

Historically, OEP was classified as intrafollicular (within the CL) or extrafollicular (within the ovarian stroma)[10,11]. However, intrafollicular OEP is seen rarely in practice and widely followed clinical guidelines stipulate that an OEP should be visualized on ultrasound separately to a CL[1,12]. Microscopically, OEP is characterized by the presence of chorionic villi and trophoblastic tissue adjacent to ovarian stroma[13,14].

Pathophysiology

A histopathological study showed that ovarian gestational sites, compared to a normally sited pregnancy, undergo an accentuated inflammatory process and subsequent immune response[15]. This leads to increased local adhesivity, favoring pregnancy implantation at this site. The presence of macrophages and mastocytes can provide growth factors for pregnancy tissue development and activate local angiogenesis. It has also been shown that trophoblast cells in OEP demonstrate atypical hypercellularity and hypovascularity[15].

Clinical presentation and prognosis

OEP presents similarly to TEP in that affected women may experience abdominal pain and/or vaginal bleeding in early pregnancy. However, a larger proportion of OEPs present with collapse and hemodynamic instability due to significant hemoperitoneum[16,17]. One study found that 80% of OEPs had hemoperitoneum on ultrasound[8] and another found up to 30% presented with circulatory collapse[14]. Despite the higher volume of blood loss and greater need for blood transfusion, mortality rates are low in settings with access to diagnostic and emergency surgical services.

METHODS

This was a retrospective case–control study of women with OEP compared to those with TEP, who presented to University College London Hospital (UCLH), London, UK, between December 2010 and February 2021. The Early Pregnancy Unit (EPU) at UCLH is a tertiary referral center that receives walk-ins, as well as referrals from general practice, emergency care and other EPUs from across the country. We reviewed the records of all women diagnosed with OEP who presented during the study period. We also randomly selected 100 cases of TEP from a dedicated database, using an online computer random number generator (https://www.random.org). Clinical information, ultrasound images, surgical notes and histological results were retrieved from the database. Data were anonymized and stored securely according to General Data Protection Regulations.

We followed European Society of Human Reproduction and Embryology (ESHRE) terminology to define ectopic pregnancy[1]. We defined OEP as a pregnancy located completely or partially within the ovarian parenchyma that was inseparable from the ovary, and which, on transvaginal ultrasound scan, was seen separately to a CL, if a CL was within the ipsilateral ovary. A CL could be cystic or solid and is characterized by a thick, moderately echogenic wall. When cystic, it usually contains echogenic fluid. On color Doppler, a CL appears highly vascular with circumferential blood flow that is often referred to as the ring of fire (Figure 2b). In comparison, the wall of the gestational sac is better defined and is typically hyperechogenic, but it may also show mild cystic changes. Blood supply tends to be high, but less so compared with the CL (Figure S1). TEP was defined as a pregnancy located within any part of the Fallopian tube, including interstitial, isthmic and ampullary pregnancies. Time to resolution was defined as the number of days until human chorionic gonadotropin (hCG) levels declined to < 20 IU/L.

Our reference standard for diagnosis was surgical confirmation of ectopic pregnancy with histological verification of pregnancy tissue. For ectopic pregnancy managed conservatively, diagnosis was made on an ultrasound scan performed by at least two gynecologists with expertise in diagnosing early pregnancy complications.

The extent of hemoperitoneum on ultrasound was classified in a standardized way[18]. Mild hemoperitoneum was defined as presence of echogenic fluid in the pouch of Douglas. Moderate hemoperitoneum was defined as presence of blood clots within the pouch of Douglas. Severe hemoperitoneum was defined as presence of blood clots and echogenic fluid in both the pouch of Douglas and uterovesical fold (Figure 3).

Surgical treatment was advised for all OEPs, due to the recognized risk of rapid blood loss in the case of rupture. Surgery was performed by the on-call clinical team with expertise in minimally invasive surgery. The

surgical diagnosis of OEP was made when a pregnancy was seen to have implanted on or within the ovary[19]. Indications for surgery for TEP were presence of a live embryo, high or rising hCG, hemoperitoneum, worsening abdominal pain and the patient's choice.

The objectives of the study were to examine demographic features, risk factors, clinical presentation, ultrasound findings and outcomes of OEPs and then compare them to a randomly selected group of TEPs. Outcomes of interest included estimated blood loss at surgery, blood transfusion rate, total number of days admitted in hospital (including day of surgery), length of follow-up and future pregnancy outcome.

The normality of distribution for baseline variables was tested using the Shapiro–Wilk test. The mean ± SD was calculated for normally distributed continuous variables. The median (interquartile range (IQR)) was calculated for continuous variables that were not normally distributed. Categorical variables are presented as *n* (%). Continuous outcomes were compared using the independent *t*-test for normally distributed data and Mann–Whitney *U*-test for non-normally distributed data. Categorical outcomes were compared using the chi-square test or Fisher's exact test. Odds ratios (OR) with 95% CI were calculated. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS; IBM Corp., Armonk, NY, USA).

We sought advice from the National Health Service Research Ethics Committee and the local ethics committee and were advised that formal ethics approval was not needed for this study, as the data had already been collected as part of routine care and were anonymized and analyzed within the care team.

RESULTS

During the study period, 45 021 women attended the EPU with clinical symptoms suggestive of early pregnancy complications. Of those, 1562 (3.5%) women were diagnosed with an ectopic pregnancy, of which 1401 were extrauterine, including 1378 tubal, 20 ovarian and three abdominal pregnancies. A total of 814 women with an extrauterine pregnancy underwent surgical treatment, of which 19 (2.3%) were diagnosed with an OEP at surgery.

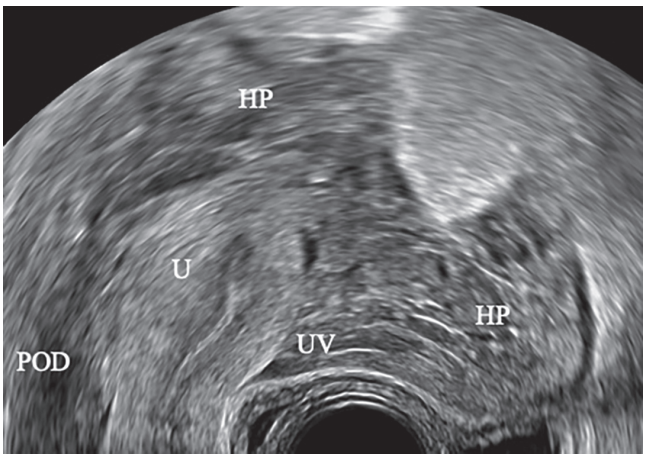

Figure 3 Transvaginal ultrasound image in longitudinal view of uterus (U), showing echogenic fluid and blood clots in pouch of Douglas (POD) and uterovesical fold (UV), indicating severe hemoperitoneum (HP).

The demographic characteristics of women diagnosed with OEP and those diagnosed with TEP are shown in Table 1. The groups were balanced for maternal age, gestational age, gravidity and parity. There was no significant difference in the proportion of women who had undergone previous uterine or other pelvic surgery between the two groups (Table 2). There was also no difference in the proportion of smokers, users of intrauterine contraceptive devices (IUCD), those with a history of gynecological infection (pelvic inflammatory disease, chlamydia, gonorrhea) and those who conceived using assisted reproductive technology (ART). OEPs were more likely to present with abdominal pain as the only symptom compared with TEPs (12/20 (60%) *vs* 13/100 (13%); OR, 10.0 (95% CI, 3.45–29.20); $P < 0.01$) (Table 3).

Diagnosis

A total of 101/120 (84%) extrauterine ectopic pregnancies included in the study were identified correctly on the initial ultrasound scan, whilst the rest required between one and four follow-up examinations until the diagnosis was reached. Of note, 15/20 (75%) OEPs were diagnosed correctly on the first scan. The remaining 5/20 (25%) were misdiagnosed as TEP, but found to be OEP at surgery (Figure 4). In two of these cases, blood clots surrounding the ectopic pregnancy were misdiagnosed as hematosalpinges (Figure S2) and, in another case, there was severe hemoperitoneum with blood extending to Morrison's pouch.

During the study period, there were also four false-positive diagnoses of OEP on preoperative ultrasound, of which all were found to be TEP at surgery (Figure S3). In all such cases, the Fallopian tube containing the pregnancy was noted to be adherent to the ovary, both on ultrasound and at surgery.

The proportion of OEPs presenting as a gestational sac containing an embryo with cardiac activity (Figure S4)

Table 1 Demographic characteristics of women with ovarian ectopic pregnancy (OEP) and those with tubal ectopic pregnancy (TEP)

Characteristic	*OEP (n = 20)*	*TEP (n = 100)*
Maternal age (years)	31.8 ± 5.2	30.5 ± 5.1
Gestational age (days)*	50 (42–58)	44 (40–53)
Gravidity		
1	6 (30)	42 (42)
2	7 (35)	24 (24)
≥ 3	7 (35)	34 (34)
Parity		
0	9 (45)	66 (66)
1	8 (40)	19 (19)
≥ 2	3 (15)	15 (15)

Data are given as mean ± SD, median (interquartile range) or *n* (%).
*Data were missing for one woman with OEP and 11 women with TEP.

was higher compared to TEPs (3/20 (15%) *vs* 2/100 (2%); OR, 8.7 (95% CI, 1.34–55.65); $P = 0.02$). The median endometrial thickness in OEP was 9.0 (IQR, 6.0–13.1) mm, which was similar to that in TEP (7.9 (IQR, 5.1–11.2) mm; $P = 0.19$). The location and number of CLs were recorded in 113/120 (94%) cases (18 OEP and 95 TEP). Bilateral CL was seen in 5/18 (28%) OEPs and 9/95 (9%) TEPs (OR, 3.6 (95% CI, 1.06–12.68); $P = 0.04$). In 14/18 (78%) OEPs, a CL was seen ipsilateral to the ectopic sac, compared with 67/95 (71%) TEPs ($P = 0.5$). In all cases in which a CL was recorded, the OEP was seen as a structure separate to it with distinctive blood supply on color Doppler examination (Figure S5). Hemoperitoneum was present more frequently (Figure 3), with a tendency to be more severe, in cases of OEP compared with TEP (9/20 (45%) *vs* 8/100 (8%); OR, 9.4 (95% CI, 3.01–29.40); $P < 0.01$) (Table 3). OEPs had significantly higher median serum hCG (3576 (IQR, 1266–6105) IU/L *vs* 847 (IQR, 247–1772) IU/L; $P < 0.01$) and serum progesterone (22.8 (IQR, 13.9–51.0) nmol/L *vs* 13.9 (IQR, 6.2–28.1) nmol/L; $P = 0.02$) compared with TEPs.

Treatment

Treatment and outcomes are shown in Table 4. Of the 20 cases of OEP, 19 (95%) were treated surgically. The remaining patient was advised to have surgical treatment, but declined. She was managed expectantly as an outpatient until her serum hCG returned to the prepregnancy level 6 weeks later. Of those treated surgically, 18/19 (95%) underwent laparoscopic excision of OEP and the remaining patient had laparoscopic wedge

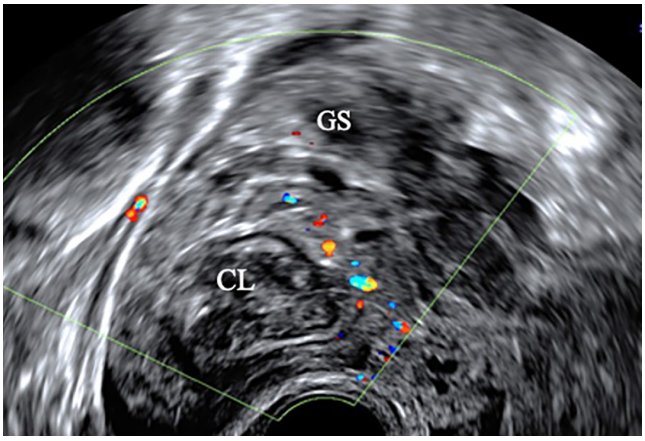

Figure 4 Transvaginal ultrasound image with color Doppler in transverse view of false-negative ovarian ectopic pregnancy that was described as tubal ectopic pregnancy. Corpus luteum (CL) is seen within ovary and gestational sac (GS) appeared to be adjacent to ovary. At surgery, this was confirmed to be an ovarian ectopic pregnancy.

Table 2 Risk factors associated with ovarian ectopic pregnancy (OEP) and tubal ectopic pregnancy (TEP)

Risk factor	*OEP (n = 20)*	*TEP (n = 100)*	*OR (95% CI)*	P
Conception using ART	3 (15)	6 (6)	2.7 (0.62–12.00)	0.18
History of TEP	1 (5)	5 (5)	1.0 (0.11–9.05)	> 0.99
History of SMM/STOP	7 (35)	18 (18)	2.5 (0.85–7.02)	0.09
History of CS	1 (5)	11 (11)	0.4 (0.05–3.57)	0.44
IUCD *in situ*	1 (5)	2 (2)	2.6 (0.22–29.89)	0.45
History of pelvic surgery	1 (5)	9 (9)	0.5 (0.06–4.45)	0.56
Tubal pathology	0 (0)	2 (2)	Indeterminable	—
Smoker	2/13 (15)	13/60 (22)	0.7 (0.13–3.35)	0.61
Previous PID/chlamydia/gonorrhea	3/17 (18)	9/86 (10)	1.8 (0.44–7.63)	0.61
Infertility/subfertility	3 (15)	9 (9)	1.7 (0.41–6.84)	0.47

Data are given as *n* (%) or *n*/*N* (%), unless stated otherwise. ART, assisted reproductive technology; CS, Cesarean section; IUCD, intrauterine contraceptive device; OR, odds ratio; PID, pelvic inflammatory disease; SMM, surgical management of miscarriage; STOP, surgical termination of pregnancy.

Table 3 Symptoms at presentation and ultrasound findings associated with ovarian ectopic pregnancy (OEP) and tubal ectopic pregnancy (TEP)

Variable	*OEP (n = 20)*	*TEP (n = 100)*	*OR (95% CI)*	P
Symptom				
Abdominal pain only	12 (60)	13 (13)	10.0 (3.45–29.20)	< 0.01
Vaginal bleeding only	1 (5)	17 (17)	0.3 (0.03–2.05)	0.20
Abdominal pain and vaginal bleeding	6 (30)	68 (68)	0.2 (0.07–0.57)	< 0.01
Asymptomatic	1 (5)	2 (2)	2.6 (0.22–29.89)	0.45
Ultrasound finding				
Embryo FH+	3 (15)	2 (2)	8.7 (1.34–55.65)	0.02
Hemoperitoneum on scan				
None	8 (40)	63 (63)	0.4 (0.15–1.05)	0.06
Mild	1 (5)	21 (21)	0.2 (0.03–1.57)	0.12
Moderate	2 (10)	8 (8)	1.3 (0.25–6.52)	0.77
Severe	9 (45)	8 (8)	9.4 (3.01–29.40)	< 0.01

Data are given as *n* (%), unless stated otherwise. FH+, fetal heart activity; OR, odds ratio.

resection of the ovary. All procedures were performed or supervised by gynecologists with expertise in intermediate or advanced laparoscopic surgery. Most patients (18/19 (95%)) were treated surgically within 12 h of the diagnosis and the remaining patient was treated the following day. Most procedures were performed between 8 am and 8 pm.

In comparison, 53/100 (53%) TEPs had initial expectant management and 47/100 (47%) were treated by primary surgery. Of those expectantly managed, 29/53 (55%) were successful and 24/53 (45%) failed, with 23 having surgery and one patient opting for medical treatment with methotrexate. A total of 70/100 (70%) TEPs underwent surgical management: 66/70 (94%) had laparoscopic salpingectomy, 3/70 (4%) had laparoscopic salpingotomy and 1/70 (1%) had laparoscopic retrieval of TEP expelled spontaneously from the Fallopian tube.

Estimated blood loss at surgery was documented in the operative notes in 17/19 (89%) OEPs. This ranged from 20 to 2000 mL, with 9/17 (53%) cases having an estimated blood loss of ≥ 500 mL (Table 4). One patient had severe hemoperitoneum on preoperative ultrasound (1000 mL) and a total blood loss of 1500 mL at surgery. She was the only patient with OEP who had a blood transfusion and was given 2 units of red blood cells. In comparison, 6/62 (10%) TEPs with documented blood loss at surgery had ≥ 500 mL hemoperitoneum and none of them required a blood transfusion. OEPs had a higher median blood loss at surgery compared with TEPs (700 (IQR, 200–1500) mL *vs* 100 (IQR, 50–250) mL; $P < 0.01$) and were less likely to have ≤ 499 mL of blood loss (8/17 (47%) *vs* 56/62 (90%); OR, 0.1 (95% CI, 0.03–0.34); $P < 0.01$).

The majority of both OEPs (63%) and TEPs (83%) were admitted to hospital for a total of 2 days. OEPs were more likely to stay for ≥ 4 days compared with TEPs (4/19 (21%) *vs* 1/69 (1%); OR, 18.1 (95% CI, 1.89–174.04); $P = 0.01$).

Follow-up and time to resolution

Time to resolution was defined as the number of days until hCG levels fell to < 20 IU/L. Among cases of OEP, 18/20 (85%) were advised to have follow-up with serial serum hCG as outpatients (two had follow-up elsewhere). The median time to resolution in OEP cases was 19 (IQR, 12–26) days (Table 4). Of TEPs treated surgically, 3/70 (4%) had laparoscopic salpingotomy and were followed up with serial serum hCG. Time to resolution from laparoscopic salpingotomy until serum hCG < 20 IU/L was 10, 12 and 15 days. Among TEPs that were managed expectantly, median hCG resolution time was 21 (IQR, 13–30) days.

Future pregnancy outcome

We obtained future pregnancy outcome for seven women with OEP, all of whom had an uncomplicated pregnancy followed by a live birth. Of 45 women with TEP and a known future pregnancy outcome, 33 (73%) had a live birth, which was not significantly different compared with OEP (OR, 5.6 (95% CI, 0.30–105.40); $P = 0.25$). Of the remaining TEPs, 6/45 (13%) had a miscarriage before 12 weeks' gestation, 4/45 (9%) had a recurrent TEP and 2/45 (4%) had a termination of pregnancy.

DISCUSSION

Main findings

We have shown that the majority of OEPs can be diagnosed preoperatively on an initial transvaginal ultrasound scan. Compared with TEP, OEP was more likely to present with abdominal pain as the only symptom. On ultrasound scan, a higher proportion of OEPs contained an embryo and presented with multiple CLs compared to TEPs. OEP was also associated with higher pre- and intraoperative blood loss compared with TEP. Early diagnosis facilitated better surgical planning and the utilization of minimally invasive, semielective interventions by appropriately skilled clinicians, which minimized severe adverse outcomes, such as loss of an ovary and need for blood transfusion. All surgically managed OEPs were treated successfully and none required additional intervention.

Table 4 Outcome of patients with ovarian ectopic pregnancy (OEP) or tubal ectopic pregnancy (TEP)

Outcome	*OEP (n = 20)*	*TEP (n = 100)*	*OR (95% CI)*	P
Management				
Surgical	19 (95)	70 (70)	8.1 (1.04–63.63)	0.04
Medical	0 (0)	1 (1)	Indeterminable	—
Expectant	1 (5)	29 (29)	0.1 (0.02–1.01)	0.05
EBL at surgery				
≤ 499 mL	8/17 (47)	56/62 (90)	0.1 (0.03–0.34)	< 0.01
500–999 mL	4/17 (24)	5/62 (8)	3.5 (0.83–14.90)	0.09
≥ 1000 mL	5/17 (29)	1/62 (2)	23.3 (2.49–218.25)	< 0.01
Length of hospital stay				
1 day	0/19 (0)	1/69 (1)	Indeterminable	—
2 days	12/19 (63)	57/69 (83)	0.4 (0.12–1.11)	0.07
3 days	3/19 (16)	10/69 (14)	1.1 (0.27–4.50)	0.89
≥ 4 days	4/19 (21)	1/69 (1)	18.1 (1.89–174.04)	0.01
Time to resolution (days)	19 (12–26)	21 (12–30)	—	0.56

Data are given as *n* (%), *n/N* (%) or median (interquartile range), unless stated otherwise. EBL, estimated blood loss; OR, odds ratio.

Limitations

A limitation of this study is that the number of cases is relatively low, owing to the rarity of OEP. The small sample size resulted in wide 95% CIs, leading to imprecision of the estimated effect. A small number of cases had missing outcomes, which is a recognized limitation of retrospective studies. In addition, the sensitivity of ultrasound diagnosis in women undergoing surgery was only 75%. In view of this, it is possible that, among women who were managed conservatively, there were cases of OEP which were misclassifed as TEP.

Risk factors

ART has been reported as a risk factor for OEP[6,20–22], with theories suggesting that high-volume culture medium or stimulation of uterine contractions from a difficult embryo transfer can lead to retrograde movement of embryos through the Fallopian tubes and into the ovary[8,23–25]. Other explanations include ovarian injury after oocyte retrieval, facilitating embryo implantation[26], and higher number of spermatozoa reaching the ovary following intrauterine insemination[11,27]. Pelvic adhesions, as a result of previous pelvic infection, surgery or endometriosis, are thought to disrupt ovum release, facilitating implantation within the ovary[12,28]. However, evidence for this is inconclusive[17,22,29–31]. IUCDs have also been associated with an increased risk of OEP[3,6,14,22,32,33], thought to be due to altered tubal motility facilitating ovarian implantation[28]. This study did not demonstrate an increased risk of OEP associated with ART, pelvic adhesions or IUCD, although this could be due to the small sample size.

Diagnosis

This study had a high preoperative detection rate of OEP (75%). Ultrasound examinations in our clinic are performed by highly skilled Level-III operators who routinely use color Doppler and palpation of pelvic organs with the ultrasound probe when assessing women presenting with suspected early pregnancy complications. These are likely to be the key factors contributing to the high sensitivity of ultrasound diagnosis we observed. Most studies on OEP report a lower preoperative detection rate of between 0% and 33%[3,8,14,29,34,35]. One study identified 75% (9/12) OEPs preoperatively, but the article focused on surgical management with little information on how the preoperative diagnosis was made[36].

Key ultrasound features in this study were that all OEPs were located within the ovarian stroma and there was an inability to separate the pregnancy from the ovary on palpation. It is also important to use color Doppler to identify peritrophoblastic flow separate to the CL (Figure 2b). Although some clinicians rely on the presence of a gestational sac or embryo to diagnose an OEP[3,21,29], the absence of these structures does not preclude a diagnosis of OEP, highlighted in this study, which showed that a proportion of OEPs presented as solid swellings with no discernible gestational sac (Figure S6). Visualizing the Fallopian tube walls surrounding blood and clots in the form of a hematosalpinx can also help differentiate TEP from OEP (Figure S7). Adhesions between a TEP and ovary can sometimes make it difficult to differentiate a TEP from an OEP. This is not a frequent problem and, over the period of 11 years covered by this study, we recorded only four false-positive diagnoses of OEP among 814 women who underwent surgery for an extrauterine pregnancy, with pelvic adhesions fixing the TEP to the ipsilateral ovary. However, it is important to stress that preoperative ultrasound diagnosis of OEP is more difficult compared with other more common types of ectopic pregnancy, and it should be always considered in patients presenting with a live ectopic pregnancy and significant intra-abdominal bleeding.

Blood loss and treatment

OEP is associated with significant hemoperitoneum on ultrasound scan[6,8,14,29,36]. In one of the largest studies to date, only 2.5% of OEPs were identified sonographically, but 80% had hemoperitoneum triggering surgical intervention[8]. Finding an OEP amongst severe hemoperitoneum can be challenging on ultrasound (Figure S8). Greater blood loss in OEP compared with TEP could be explained by high ovarian vascularity (Figure S9). This provides better conditions than do Fallopian tubes for an extrauterine gestation to develop and grow quickly, reflected in higher serum hCG levels and a higher proportion of pregnancies which contain a live embryo. In addition, difficulty with timely diagnosis leads to delay in treatment, increasing the risk of intra-abdominal hemorrhage.

Prompt surgical intervention is required, with the trend moving away from laparotomy towards laparoscopy[34,36,37]. Surgical excision of the ectopic pregnancy, while preserving the ovary, is ideal. Ovarian wedge resection is sometimes necessary in larger, more advanced pregnancies, whilst oophorectomy should be reserved as a last resort when faced with uncontrollable bleeding. Previous studies have reported a 5–28% rate of oophorectomy[3,4,28,35,36,38] and a 10–25% rate of blood transfusion[3,14], compared with a 0% rate of oophorectomy and a 5% rate of blood transfusion among OEP cases in this study. This reduction in morbidity could be attributed to earlier diagnosis, allowing optimization of treatment and ensuring the presence of adequately skilled operating surgeons.

Conclusions

This study highlights key clinical characteristics and ultrasound features associated with OEP that can be used as a reference for clinicians who may not otherwise encounter this rare condition. Palpation and color Doppler are important components of ultrasound assessment, and the finding of an ectopic pregnancy containing an embryo, in conjunction with severe

hemoperitoneum, should prompt the clinician to consider OEP in the differential diagnosis. We have shown that in a dedicated early pregnancy setting, the majority of OEPs could be detected on ultrasound scan at the initial visit, facilitating optimal surgical treatment and reducing the risk of blood transfusion and oophorectomy.

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SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

Figure S1 Transvaginal ultrasound image with color Doppler demonstrating lesser vascularity of ovarian ectopic pregnancy (OEP) compared with hemorrhagic corpus luteum (CL).

Figure S2 Transvaginal ultrasound image in longitudinal view of pelvis with hemoperitoneum (HP) in the form of a large blood clot located in pouch of Douglas behind uterus (U). HP was misdiagnosed as hematosalpinx, but note absence of Fallopian tube surrounding blood clot (arrows).

Figure S3 Color Doppler (a) and grayscale (b) transvaginal ultrasound images of false-positive ovarian ectopic pregnancies demonstrating: (a) absence of blood supply (arrow) between ectopic pregnancy (EP) and corpus luteum (CL); and (b) gestational sac (GS) that appears to be implanted within ovarian stroma. In hindsight, Fallopian tube (arrow) can be seen next to ectopic pregnancy.

Figure S4 Transvaginal ultrasound images demonstrating ectopic pregnancy morphology Type I: (a) gestational sac (GS), yolk sac (YS) and embryo (E) are visible; and (b) cardiac activity is visible on M-mode.

Figure S5 Transvaginal ultrasound image with color Doppler of ovarian ectopic pregnancy, showing corpus luteum (CL) seen separately to gestational sac (GS), with distinctive blood supply between the two structures.

Figure S6 Transvaginal ultrasound images with color Doppler of ovarian ectopic pregnancy (OEP) morphology Type V (inhomogeneous inconglomerate), which is seen separately to solid (a) or cystic (b) corpus luetum (CL).

Figure S7 Grayscale transvaginal ultrasound image in transverse view of hematosalpinx (HS) containing gestational sac (GS) surrounded by Fallopian tube.

Figure S8 Grayscale transvaginal ultrasound image of pelvis in transverse view, showing ovarian ectopic pregnancy (OEP) surrounded by hemoperitoneum (HP).

Figure S9 Transvaginal ultrasound image showing gestational sac (GS) within ovarian stroma (O). Color Doppler demonstrates high vascularity of ovarian ectopic pregnancy.

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Embarazo ectópico ovárico: características clínicas, diagnóstico ecográfico y tratamiento

RESUMEN

Objetivo. Comparar las características clínicas, ecográficas y bioquímicas del embarazo ectópico ovárico (EEO) con las del embarazo ectópico tubárico (EET).

Métodos. Se trata de un estudio retrospectivo de casos y controles de mujeres con EEO y con EET atendidas en un único centro entre diciembre de 2010 y febrero de 2021. El EEO se definió como un embarazo localizado total o parcialmente en el parénquima ovárico, visto por separado de un cuerpo lúteo, si éste estaba presente en el ovario ipsilateral. Se compararon las características demográficas, los factores de riesgo, la presentación clínica, los hallazgos ecográficos y los resultados, como la pérdida de sangre en la cirugía, la necesidad de transfusión sanguínea, la duración de la estancia hospitalaria, el seguimiento y el resultado futuro del embarazo, entre los casos de EEO y EET.

Resultados. En total, se identificaron 20 mujeres con EEO y se compararon con 100 mujeres con EET. En la primera ecografía se diagnosticaron correctamente un total de 15/20 (75%) EEO. No hubo diferencias entre los grupos en cuanto a la edad materna, la edad gestacional, la gravidez, la paridad o los factores de riesgo. En comparación con el EET, el EEO tenía más probabilidades de presentar dolor abdominal sin hemorragia vaginal (12/20 (60%) frente a 13/100 (13%); razón de momios (RM), 10,0 (IC 95%, 3,45–29,20); P<0.01), contener un embrión con actividad cardíaca (3/20 (15%) frente a 2/100 (2%); RM, 8,7 (IC 95%, 1,34–55,65); P=0.02) y presentar hemoperitoneo grave en la ecografía (9/20 (45%) frente a 8/100 (8%); RM, 9,4 (IC 95%, 3,01–29,40); P<0.01), y tenía un mayor volumen de pérdida de sangre en la cirugía (mediana, 700mL frente a 100 ml; P<0.01). Todos los EEO tratados quirúrgicamente fueron tratados mediante laparoscopia con éxito (18 escisiones, una resección en cuña) con preservación del ovario. Sólo un caso (5%) de EEO requirió una transfusión sanguínea.

Conclusiones. El EEO tiene más probabilidades que el EET de contener un embrión y de presentar un hemoperitoneo grave. En un entorno dedicado al embarazo precoz, la mayoría de los EEO se detectaron en una ecografía en la visita inicial, lo que facilitó un tratamiento quirúrgico mínimamente invasivo óptimo, lo cual redujo el riesgo de transfusión sanguínea y ovariectomía. Estos hallazgos pueden servir de referencia para médicos clínicos que no se encuentren habitualmente con esta rara afección.

卵巢妊娠：临床特征、
超声诊断和处理

摘要

目的 比较卵巢妊娠（OEP）与输卵管妊娠（TEP）的临床、超声和生化特征。
方法 本研究为回顾性病例对照研究，研究对象为2010年12月至2021年2月期间在同一医疗机构就诊的卵巢妊娠妇女和输卵管妊娠妇女。卵巢妊娠是指完全或部分在卵巢实质内发生的妊娠，与同侧卵巢内形成的黄体相区别。研究比较了 OEP 和 TEP 病例的人口统计学特征、风险因素、临床表现、超声检查结果以及手术失血量、输血需求、住院时间、随访和未来妊娠结果等结局。
结果 共确定 20 名 OEP 妇女，并与 100 名 TEP 妇女进行了比较。在第一次超声检查中，共有 15 例（共 20 例，占75%）OEP 患者被正确诊断。两组孕妇的年龄、胎龄、孕次、产次或风险因素均无差异。与 TEP 组相比，OEP 组更有可能出现以下情况：不伴阴道出血的腹痛，（12/20（60%） vs 13/100（13%）；比值比（OR）10.0（95%CI，3.45-29.20）；P<0.01），含有胚胎且有心管搏动（3/20（15%） vs 2/100（2%）；OR 8.7（95%CI，1.34-55.65）；P=0.02），超声检查有严重腹腔积血（9/20（45%） vs 8/100（8%）；OR 9.4（95%CI，3.01-29.40）；P<0.01），手术时失血量较多（中位数，700mL vs 100 mL；P<0.01）。所有经手术治疗的 OEP 病例都成功进行了腹腔镜治疗（18 例切除，1 例楔形切除），并保留了卵巢。只有一例（5%）OEP 需要输血。
结论 OEP 比 TEP 更有可能含有胚胎，并伴有严重的腹腔积血。在专门的孕早期医疗环境中，大多数 OEP 病例都能在初诊时通过超声检查发现，这有利于实施最可取的微创手术治疗，降低输血和输卵管切除风险。本研究结果可供未遇到此种罕见病情的临床医生参考。