Ovarian tumours in pregnancy: a literature review

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ABSTRACT

Ovarian tumours in pregnancy are a diagnostic and management challenge that is increasingly being faced by the clinician. While most masses are benign and resolve spontaneously, there are others that persist and indicate the need for surgical management. Ultrasound not only detects asymptomatic masses but also helps to guide their management based on presence or absence of features suspicious of malignancy. The role of tumour markers in pregnancy is limited due to their non-specific nature. Most masses treated in pregnancy are benign (most commonly dermoids), and most malignancies are either of low malignant potential or germ cell tumours, usually early stage disease. Surgical management is indicated for symptomatic masses or those with increasing size or complexity indicating possible malignancy. Both laparoscopy and laparotomy have similar results with regard to obstetric outcome. Conservative management is preferred in the remainder. MRI may help in better characterization of doubtful masses. National tumour registries can help to establish guidelines.

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1. Introduction

The advent of ultrasound use in early pregnancy for assessing fetal viability, growth and anomalies, has been an important advance in obstetric care. It has, however, resulted in increased detection of ovarian masses, which previously would not have been clinically apparent. Most ovarian masses in early pregnancy are physiological and resolve spontaneously, but some persist and the management of such cysts is variable. Masses persisting after the first trimester or found during the second trimester are generally excised to prevent torsion or rupture during pregnancy or possible obstruction during labour, and to exclude malignancy.

The risk of ovarian malignancy is rare in pregnancy, with a reported incidence between one in 12,000 and 47,000 [1]. Nevertheless it is the second most common gynaecological malignancy in pregnancy. The objective of this review is to ascertain the reported evidence on this subject, focussing on ovarian cancer, and compile recommendations derived from this information.

2. Method

A Medline database search (January 1984–November 2009) was undertaken using key words: ovarian tumour and pregnancy, ovarian mass and pregnancy (limits: human, female, adolescent, 19+, English). The flowchart for the study method is shown in Fig. 1. Of the 33 relevant papers, six were prospective and the rest retrospective. Results in the form of prevalence, type of tumour,
timed of diagnosis, symptoms during pregnancy, type of management, nature and indication of surgery, chemotherapy and pregnancy outcomes were evaluated for selected studies. Papers with fewer than 10 cases were excluded to ensure homogeneity of care in larger settings, as were repeat updated papers, or those without histological confirmation.

3. Results

The combined reports revealed the prevalence of adnexal masses in pregnancy to range from 1/76 to 1/2328 deliveries. Not surprisingly, the studies based purely on ultrasound detection of adnexal masses [2–5] in pregnancy showed a higher prevalence of 1/19–1/88. The percentage of malignant tumours, both low malignant potential (LMP) and ovarian cancer, ranged from 2.15% to 13.5% of the total detected adnexal masses. Studies reporting only malignant ovarian tumours [6–10] found an incidence of 0.073–0.11 cases per 1000 deliveries. Ultrasound based studies found a lower incidence of malignancy, ranging from nil to 3.6%.

Pregnancy trimesters were defined as first trimester (T1) – up to 12 weeks, second trimester (T2) – 13–28 weeks and third trimester (T3) – 29–42 weeks. For ease of analysis and to obtain meaningful results, the studies were classified into four groups:

1. Studies including all patients who were detected with an adnexal mass during pregnancy or postpartum
2. Studies including only surgically managed cases (excluding masses which spontaneously resolved)
3. Studies comparing open and laparoscopic surgery
4. Studies with incidental detection of mass during caesarean section

3.1. Studies including all patients who were detected with an adnexal mass during pregnancy or postpartum

There were 10 studies which reported adnexal masses detected and followed up in pregnancy up to the point of definite management (either cyst resolution or surgery), of which four were prospective and six retrospective (Table 1). These studies included patients with masses ≥3 cm [2–4], ≥4 cm [11], ≥5 cm [12,13], ≥6 cm [14] or masses of any size.

There were 940 patients in the 10 studies. In only four studies [4,11,13,15] was the mean gestational age at diagnosis of the mass reported, which ranged from 4 to 41 weeks. Data regarding number of cases detected in each trimester were available in nine out of 10 studies (total 809 cases), but not in that by Thornton and Wells [16]. Masses were detected in the first trimester in 159 (19.6%), in the second trimester in 75 (9.3%), in the third trimester or at term in 157 (19.4%) patients, and postpartum in 15 (1.8%).

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Four studies [4,5,11,13] reported on detection of masses in the first and second trimesters together and this included 403 patients (49.8%). Thus the majority of masses were detected in the first half of pregnancy.

Data regarding symptoms were not available for one study [16]. In the remaining studies, consisting of 809 patients, 529 (65.4%) were asymptomatic; pain was recorded in 136 (16.8%) and other symptoms like bleeding/obstruction/rupture were recorded in 73
In the six retrospective studies [11–16] with 560 patients, the cysts resolved with conservative management or did not require surgery in 172 (30.7%) cases, elective surgery was undertaken in 178 (31.7%) cases and emergency surgery in 210 (37.5%) cases. These included both antenatal and postpartum operations. Histopathology was available for 548 cysts removed at surgery. Notable were 17 borderline ovarian tumours (3.1%) and 14 malignant ovarian tumours (2.5%). These included three mucinous cystadenocarcinomas, two each of Brenner tumour, serous cystadenocarcinoma, embryonal cell carcinoma, endodermal sinus tumour and endometrioid adenocarcinoma, and one case of mixed germ cell tumour. Specific characteristics relating to a risk of malignancy were complex masses, papillary projections, solid parts, irregular capsule or border, ascites, irregular vascularity and increase in size of mass on repeat scan. The most common benign tumour in these studies was dermoid, in 190 (34.6%) cases, followed by cystadenoma in 129 (23.5%) cases.

Neonatal outcomes were not available for all studies but where recorded included five preterm births, two spontaneous abortions and eight therapeutic terminations of pregnancy, four intrauterine deaths and seven neonatal deaths. There was one maternal death.

3.2. Studies including only surgically managed cases (excluding masses which spontaneously resolved)

There were 17 studies, two prospective and 15 retrospective, reporting on 1203 cases managed surgically during pregnancy or puerperium. Five studies reported only on malignant tumours in pregnancy. These are discussed separately.

(i) Studies reporting on both benign and malignant tumours

These are shown in Table 2. Of a total of 925 cases among the 12 studies (10 cases were lost to follow up), the mean gestational age at diagnosis was reported in seven studies, which ranged from 5 to 42 weeks. Data were available for 487 patients regarding the gestation at diagnosis. In 173 (35.5%) cases masses were diagnosed in T1, in 60 (12.3%) cases in T2, in 180 (36.9%) cases in T3 or at the time of caesarean and in 65 (13.3%) cases a postpartum diagnosis was made. Fifteen cases (3%) were diagnosed in T1 and T2 (not specified separately). Thus, as before, most masses were detected in the first half of pregnancy. Six studies did not report trimester wise data [19,20,22,23,27,28].

Symptomatology was not reported in one study [24]. In the remaining 11 studies with 825 patients, 653 (79.1%) were asymptomatic, 161 (18.4%) presented with acute pain, while 11 (1.2%) presented with other symptoms. Torsion rates were not available for two studies [22,26] but the cumulative torsion rate from the other studies with 632 patients was 14.2% (total 90 cases).

Mean gestational age at surgery was reported in seven studies as between 4 and 41 weeks [17,18,20–22,27,28]. Trimester wise data for surgery were available for nine studies with a total of 803 patients. Surgery was performed in T1 in 158 (19.7%), T2 in 306 (38.1%), T3 or at time of caesarean in 268 (33.4%) and postpartum in 73 (9.1%) cases.

### Table 1

<table>
<thead>
<tr>
<th>Study, Year</th>
<th>Duration</th>
<th>Number of cases</th>
<th>Prevalence, malignancy (%)</th>
<th>Type of study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yen et al. (2009) [11]</td>
<td>15 years</td>
<td>213</td>
<td>NR, 3.4% malignancy</td>
<td>Retrospective</td>
</tr>
<tr>
<td>Balci et al. (2008) [15]</td>
<td>6 years</td>
<td>36</td>
<td>1/440, 5.8% malignancy</td>
<td>Retrospective</td>
</tr>
<tr>
<td>Schmeler et al. (2005) [13]</td>
<td>14 years</td>
<td>59</td>
<td>1/2018, 7.9% malignancy</td>
<td>Retrospective</td>
</tr>
<tr>
<td>Condous et al. (2004) [4]</td>
<td>1 year</td>
<td>161</td>
<td>1/19, 0.62% malignancy</td>
<td>Prospective, USG</td>
</tr>
<tr>
<td>Zanetta et al. (2003) [2]</td>
<td>4 years</td>
<td>79</td>
<td>1/84, 3.6% borderline</td>
<td>Prospective, USG</td>
</tr>
<tr>
<td>Bernhard et al. (1999) [5]</td>
<td>5 years</td>
<td>102</td>
<td>1/42, 0.46% malignancy</td>
<td>Prospective, USG</td>
</tr>
<tr>
<td>Platek et al. (1995) [14]</td>
<td>6.5 years</td>
<td>31</td>
<td>1/339, no malignancy</td>
<td>Retrospective</td>
</tr>
<tr>
<td>Thornton and Wells (1987) [16]</td>
<td>10 years</td>
<td>131</td>
<td>1/346, 8.6% malignancy</td>
<td>Retrospective</td>
</tr>
<tr>
<td>Nelson et al. (1986) [3]</td>
<td>2 years</td>
<td>38</td>
<td>1/88, no malignancy</td>
<td>Prospective, USG</td>
</tr>
<tr>
<td>Struyk and Treffers (1984) [12]</td>
<td>29 years</td>
<td>90</td>
<td>1/660, 0.3% malignancy</td>
<td>Retrospective</td>
</tr>
</tbody>
</table>

NR: not reported.
Histopathology was available in 944 cases in 12 studies, as some had bilateral tumours, while 17 tumours were confirmed on visual inspection in two studies and no histopathology was available [23,28]. Of note, there were 20 tumours of LMP (2.1%) and 31 malignant ovarian tumours (3.2%). These included eight serous cystadenocarcinomas, five mucinous cystadenocarcinomas, four unspecified epithelial cancers, four immature teratomas, three each of Brenner tumour and dysgerminoma, two granulosa cell tumours and one each of embryonal cell cancer and Sertoli-Leydig tumour. The most common benign tumour, as before, was dermoid cyst in 282 (29.9%), followed by cystadenoma in 214 (22.6%) cases.

Neonatal outcomes were available for nine studies with 498 patients. A cumulative analysis showed a preterm delivery rate of 10.4% (52 cases), abortion rate of 6% (30 cases), therapeutic termination in 3.6% (18 cases), one in utero death and three neonatal mortalities (two due to anomalies in the baby). This makes an adverse pregnancy outcome of 10% excluding the preterm deliveries where the neonates survived. Chemotherapy was administered with the fetus in situ in one case with good neonatal outcome.

(ii) Studies reporting only malignant cases

In the five studies reporting only on malignant ovarian masses, there were 272 cases (Table 3). Diagnosis was in made in T1 in 22 (8%) patients, T2 in 20 (7.3%) patients, T3 in 66 (24.2%) patients and postpartum in 73 (26.8%) patients. One study [9] reported data for T1 & T2 together as 90 cases (33%). Thus, as in previous studies, most cases were diagnosed in the first half of pregnancy.

As regards stage of disease, FIGO stage was not available for 105 patients in the study by Leiserowitz et al. [9]. Of the remaining 167 patients, 135 (80.8%) were stage I, nine (5.4%) were stage II, 16 (9.6%) were stage III, three (1.7%) were stage IV, and two each (1.1%) were metastatic and unstaged disease. Thus, contrary to stage at presentation outside of pregnancy, most cases in pregnancy presented with early stage disease.

Symptoms were not reported in the study by Leiserowitz et al. [9]. In the remaining 70 patients, the most common symptom was adnexal/abdominal mass in 40 (57.1%), followed by asymptomatic mass in 18 (25.7%), pain in six (8.5%) and ascites and other constitutional symptoms in 12 (17.1%) patients. Some patients had more than one symptom. Pain, however, was the least frequent of symptoms with malignancy.

Data regarding timing of surgery were not available for one study [9]. For the remaining studies with 70 patients, surgery was performed in T1 in 17 (24.2%), T2 in 19 (27.1%), T3 or at caesarean in 20 (28.5%) and postpartum in 14 (20%) cases.

Histopathology was available for all 272 tumours. Of note, there were 131 (48.1%) borderline ovarian tumours, 67 (24.6%) germ cell tumours, 59 (21.6%) epithelial ovarian cancer and 15 (5.5%) other malignancies like pseudomyxoma, sex-cord tumours and Krukenberg tumours.

Chemotherapy was administered in six cases with the fetus in situ and in a total of 54 cases in these studies. There were no recorded adverse outcomes. Neonatal outcome was available for 198 patients diagnosed during pregnancy. There were 34 (17.1%) preterm deliveries, five (2.5%) neonatal deaths, four spontaneous and eight induced miscarriages (6%), one ectopic pregnancy, one in utero death and one baby with congenital abnormality.

Seven women died from their malignancy, all due to advanced/disseminated disease.

3.3. Studies comparing open and laparoscopic surgery

Four studies included laparoscopic surgery only and two included comparison between laparoscopic and open surgery [29,30]. All of these were retrospective and a total of 206 laparoscopic procedures and 78 laparotomies were carried out. These studies are shown in Table 4.

Mean gestation age at diagnosis was reported in three studies [29,30,32] as between 5 and 25 weeks. The mean age at surgery was available for five studies [29,31–34] and ranged from 4 to 33 weeks. Of the total 284 procedures performed, 119 (41.9%) were for persistent or enlarging cyst, 117 (41.2%) were for pain and 48 (16.9%) patients were asymptomatic. Torsion was documented in 75 (26.4%) cases.

Surgery in all cases was conservative (cystectomy/oophorectomy/detorsion/aspiration/adnexectomy). Four patients (1.8%) required conversion to laparotomy.

Histopathology was available for 261 cases as some cases with adnexal detorsion were not removed for pathology. The report was benign in the vast majority (98%), with the most common being dermoid cyst in 74 (28.3%) cases. There were four tumours of LMP and two ovarian cancers.

Neonatal outcome was reported in all studies. There were 16 (5.6%) preterm deliveries, eight spontaneous miscarriages and two therapeutic terminations (total 3.5%), five babies with anomalies and one in utero death. Of note, there was no significant difference among studies comparing laparoscopy with laparotomy.

### Table 4

<table>
<thead>
<tr>
<th>Study, Year</th>
<th>Duration</th>
<th>Number of cases</th>
<th>Type of study</th>
<th>Laparoscopy/laparotomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lee et al. (2010)</td>
<td>13 years</td>
<td>53</td>
<td>Retrospective</td>
<td>29 Laparoscopy, 24 Laparotomy</td>
</tr>
<tr>
<td>Ko et al. (2009)</td>
<td>3.5 years</td>
<td>11</td>
<td>Retrospective</td>
<td>Laparoscopy in T1 only</td>
</tr>
<tr>
<td>Yuen et al. (2004)</td>
<td>9 years</td>
<td>67</td>
<td>Retrospective</td>
<td>Laparoscopy in T2 only</td>
</tr>
<tr>
<td>Mathevet et al. (2002)</td>
<td>12 years</td>
<td>47</td>
<td>Retrospective</td>
<td>Laparoscopy in all trimesters</td>
</tr>
<tr>
<td>Soriano et al. (1999)</td>
<td>20 years</td>
<td>88</td>
<td>Retrospective</td>
<td>39 Laparoscopy in T1, 54 Laparotomy in T1 &amp; T2</td>
</tr>
<tr>
<td>Parker et al. (1996)</td>
<td>9 years</td>
<td>12</td>
<td>Retrospective</td>
<td>Laparoscopy in T1 &amp; T2</td>
</tr>
</tbody>
</table>
3.4. Studies with incidental detection of mass during caesarean section

Two studies [35,36] dealt with incidental masses removed at caesarean section which were not diagnosed preoperatively. The incidence in these studies was 1 in 447 [35] and 1 in 197 [36], respectively. A total of 183 tumours were removed. Again as before, the two most common types were dermoid cyst in 55 (30%) cases and cystadenoma in 39 (21.3%) cases. There was one serous cystadenocarcinoma. Maternal and neonatal outcomes were not reported.

4. Discussion

Definitive management strategies of ovarian masses in pregnancy have not been developed. While some obstetricians prefer elective removal in the second trimester, others profess that a conservative approach results in resolution of most masses and avoids unnecessary surgery. As ultrasound has resulted in increased detection of masses, it has also helped in better characterization of masses as physiological/pathological. Certain features on ultrasound, like septations, solid areas and papillary projections, increase suspicion for malignancy and help in guiding surgical management.

This review included over 2500 gestations reporting the management of pregnancies affected by the presence of ovarian tumours. Most of these studies were retrospective. The prevalence of adnexal masses in pregnancy varied from 1/76 to 1/2328 deliveries. Between 50% and 80% masses were detected in the first two trimesters of pregnancy. Patients were asymptomatic in 65–80% cases. With malignancy, however, patients were more likely to be symptomatic of abdominal mass (>50%), while only 25% were asymptomatic, the rest having pain or constitutional symptoms. Torsion rates were between 3% and 28% in all studies.

With conservative management, 70% of masses were noted to resolve in prospective studies, while retrospective studies reported this figure at around 30%. Where surgery was carried out electively, it was mostly in T2 or at the time of caesarean section, while the timing of emergency surgery depended on the presence of symptoms. Reasons for intervention were enlarging mass, suspicion of malignancy or acute events such as torsion, rupture or haemorrhage.

Tumour markers like CA-125 have a limited role in helping to differentiate benign from malignant tumours in pregnancy as levels increase during pregnancy [37]. In fact, CA-125 is highest during the first trimester of pregnancy, with levels up to 1250 U/ml recorded. This elevation starts between 30 and 40 days after the last menstrual period, peaks between 35 and 60 days, and starts to fall by the end of the first trimester [38].

Ultrasound assessment of masses can help to determine the risk of malignancy and guide the surgical management, although a formal risk of malignancy index [39] cannot be employed due to the low specificity of CA-125. Ultrasound features which may increase concern about malignancy are thick-walled cyst, solid or mixed cystic and solid mass, internal papillary excrescences, large amount of free fluid in the pelvis or abdomen and gradually enlarging mass. When in doubt, further evaluation by MRI scan can help to distinguish benign from malignant, with an overall accuracy of 93% for malignancy [40].

Surgical management, whether open or laparoscopic, did not have an adverse impact on the overall obstetric outcome. The extent of surgery was determined by the intra-operative diagnosis of benign or malignant tumour.

In the surgically managed cases, benign tumours constituted 92–98% of the diagnoses. The most common ones were dermoid cysts (28–35%) and cystadenomas (16–24%). Taking all the cases together, low malignant potential (borderline) tumours were almost as common as frank malignancy (172 vs 189 cases), while in the non-pregnant population, borderline tumours only form a small fraction of the total ovarian cancers. With the invasive malignancies, epithelial ovarian cancer was more common than germ cell tumours. Although in the younger age group, germ cell tumours are more common, in pregnancy epithelial ovarian cancer is more common. The majority were detected at an early stage (80% were stage I at diagnosis), which differs from the non-pregnant population. Whether pregnancy facilitated their detection early

![Fig. 2. General principles of management.](image-url)
due to antenatal ultrasounds for pregnancy viability or anomaly scanning is a point of contention. Chemotherapy has been safely administered where indicated without detrimental fetal or maternal outcome.

This review was based on a retrospective analysis of the literature over the past 25 years. During this time, the management of ovarian masses in pregnancy has varied from conservative approach to immediate surgery. This review did not consider smaller series (with less than 10 cases) or individual case reports, which may have had a different spectrum of presentation and management. This precludes the formulation of management guidelines as all cases of ovarian tumours in pregnancy are not included. Some studies dealt only with active management and may confound the results of this analysis, although most studies adopted a conservative regime, with surgical management at the onset of symptoms.

Based on the above review, the following general principles may be followed for adnexal masses in pregnancy:

- Masses causing symptoms at any time are managed surgically.
- Asymptomatic masses detected in T1 at the time of dating scan may be evaluated by ultrasound to look for features of malignancy, which if present will indicate the need for surgery. If there are no suspicious features, repeat evaluation at the time of anomaly scan (18–20 weeks) can be done. If suspicious features have developed, surgery may be undertaken, as has been traditionally done in the second trimester. If doubt exists, MRI may help in better characterization. Asymptomatic masses detected in T2 can be dealt with in a similar manner, with repeat scan at 32–36 weeks, to note any changes from before.
- Asymptomatic masses detected in T3 with no features of malignancy are best left undisturbed until evaluation at caesarean or after six weeks postpartum. If intervention is needed before fetal maturity, steroid cover should be considered. This is depicted in Fig. 2.
- National tumour registries should be established where management and outcome data of all pregnancies with adnexal masses are reported and collated to arrive at meaningful guidelines for management of this obstetric dilemma.

References