Introduction

Ectopic pregnancy remains a common cause of morbidity and mortality in women of childbearing age and its incidence continues to increase worldwide.\(^1\)\(^-\)\(^4\) The number of ultrasound examinations performed to exclude potential ectopic pregnancies, to determine the location and type of ectopic pregnancy, and to plan the appropriate therapy has also increased.\(^5\) Despite advances in both diagnosis and therapy, the early diagnosis of ectopic pregnancy (EP) continues to be problematic and must be excluded in every woman who has positive pregnancy test and having empty uterus in pelvic U/S, the diagnosis would be more difficult in the absence of the fetal pole (with or without cardiac pulsations) or yolk sac inside the suspected extra uterine gestational sac.\(^6\)\(^-\)\(^9\)

Although diagnostic laparoscopy is still considered the standard reference in the diagnosis of ectopic pregnancy, yet it doesn’t have 100% sensitivity.\(^7\)\(^-\)\(^8\)

Endovaginal sonography (TVS) is the current alternative to diagnostic laparoscopy for the diagnosis of ectopic pregnancy. It has 84.4% sensitivity, 98.9% specificity, 96.3% positive predictive value (PPV), and 94.8% negative predictive value (NPV) for accuracy in the diagnosis of EP on the basis of observing any adnexal mass except for a simple cyst or an intra-ovarian lesion.\(^6\) The addition of color duplex flow imaging to TVS allows increased sensitivity in detection of EP. More over TVS is much less invasive than many other diagnostic procedures.\(^10\)\(^-\)\(^15\)

The most highly specific finding is the identification of an extra-uterine GS that contains a yolk sac or an embryo (with or without cardiac activity). However, it is not a common finding especially in early pregnancy. On the other hand, the most common adnexal finding is an echogenic homogeneous or heterogeneous, rounded, or elongated solid structure, located outside but in proximity to the ovary. The second most common finding is the tubal ring sign of ectopic pregnancy versus corpus luteum cyst: best sonographic and color duplex predictors.

TUBAL RING SIGN OF ECTOPIC PREGNANCY VERSUS CORPUS LUTEUM CYST: BEST SONOGRAPHIC AND COLOR DUPLEX PREDICTORS

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Purpose. Our purpose was to determine the best sonographic and color Duplex predictors differentiating tubal ring of ectopic pregnancy and the corpus luteum cyst of pregnancy. Methods. Prospective study of 73 pregnant women with empty uterus and questionable adnexal cystic structure devoid of fetal pole or yolk sac were included in this study. All cases underwent comprehensive transvaginal ultrasonography. Each adnexal structure was evaluated for six specific sonographic and color Duplex characteristics: the echogenicity of the wall in comparison to the endometrium and ovary, the wall thickness and internal echotexture, percentage of wall circumference by flow and resistive index of the flow. Results. Thirty four of the 73 questionable adnexal structures were ectopic pregnancy, and 39 were corpora lutea. Hyperchoic wall than the endometrium had 100% specificity and positive predictive value for diagnosing ectopic pregnancy. Iso or hypchoic wall than the ovary had 91.2% specificity and 90% positive predictive value for diagnosing corpus luteum. Solid or turbid contents are predictive for ectopic pregnancy in contrast to clear contents which was predictive for corpus luteum. RI of less than 0.4 had a specificity of 100% for diagnosing EP, and RI of more than 0.7 had a specificity of 96.4% for diagnosis of EP. There was no significant difference in extent of the flow between the two groups. Conclusion. Echogenic cyst wall than the endometrium, thick cyst wall with turbid or solid contents, as well as resistive index less than 0.4 or more than 0.7 are useful sonographic predictors for differentiating ectopic pregnancy from corpus luteum cyst.
sign in which the fallopian tube is enlarged by products of conception, blood, and blood clots.16-18 Because many ectopic pregnancies are now being detected earlier and in an un-ruptured condition, the majority of the patients present with no or minimal symptoms, and fetal pole and distinct yolk sac may not be shown.19

The hyperechoic peripheral rim of the extraovarian tubal ring is similar in sonographic appearance to the hyperechoic ring of an early intrauterine gestational sac, in contrast to the corpus luteum cyst (CLC), which is originally thick walled intra-ovarian structure enlarged during the first trimester and regress by the end of the 12th week of gestation.20-23 A dilemma arises in a pregnant patient without a sonographically visible intrauterine pregnancy when a thick-walled adnexal cystic structure is present without clear depiction of a separate ovary. Does this represent an ectopic pregnancy or a corpus luteum within the ovary, splaying the normal ovarian tissue around it? 20

Objectives

To re-evaluate the reliability of sonographic and color Duplex features in differentiating the tubal ring of the ectopic pregnancy and corpus luteum cyst.

Patients and methods

A prospective study was undertaken of 81 pregnant ladies suspected to have an ectopic pregnancy and all had a questionable cystic adnexal structure devoid of fetal pole or yolk sac by initial TVS. Ectopic pregnancy was suspected by clinical history of amenorrhea, positive pregnancy test, and the absence of intrauterine pregnancy on initial TVS despite their gestational (menstrual) age or high HCG concentrations. All patients underwent comprehensive TVS in our institution between June 2002 and August 2005 in order to re-evaluate the adnexal cystic structure.

All patients were clinically stable and asymptomatic or minimally symptomatic. Symptoms observed were minimal vaginal bleeding (n = 42) and lower abdominal discomfort (n = 33). All TVS were performed with ATL system (HDI Ultra mark) or Philips (HDI 5000 SONOCT). Using 5-9 MHz frequency transducer. Obtaining grey scale B mode and color Duplex images. The lowest used Duplex flow sensitivity on both machines was 5 cm/s. Supra-pubic examination was performed only if needed to obtain large field of view in confirmatory basis.

Each questionable cystic adnexal structure was evaluated for 6 sonographic and color Duplex characteristics: 1- The echogenicity of the wall in comparison with that of the endometrial lining. 2- The echogenicity of the wall in comparison with that of the ovarian parenchyma. 3- The average thickness of the cyst wall in 2 planes. 4- The echotexture within the cystic cavity. 5- Percentage of the wall circumference with flow (percentage of ring of fire). 6- Resistive index (RI) of that flow. If more than cystic adnexal structure were noted, the apparently extra-ovarian structure with the most echogenic wall was only included.

The echogenicity of the wall was categorized as (1) hypoechoic, (2) isoechoic and (3) hyperechoic than the endometrium or the ovary. Only the anterior and lateral walls were analyzed, posterior wall echogenicity was not used because of the potential variation in increased sound transmission through the cystic structure. The wall thickness was categorized as (1) thin i.e. ≤ 4 mm and (2) thick i.e. > 4 mm. The echo texture within the cystic cavity was described as (1) clear i.e. completely an-echoic, (2) lacy i.e. multiple thin septations in a reticular pattern, and (3) solid/turbid if there was nonvascular soft tissue within the cyst or had ground glass appearance. The percentage of ring circumference with the flow was categorized as (1) none, (2) low flow i.e. less than 50%, (3) high flow i.e. equal or more than 50%. The resistive index of the flow was categorized as (1) low-threshold RI i.e. less than 0.4 (2) intermediate-threshold RI i.e. from 0.4 to 0.7 and (3) high-threshold RI i.e. more than 0.7

All cases were planned to do conservative management & follow up of the clinical picture, B-hCG level and TVS findings. According to the result of the management, the patients were classified to four groups. First group: (26 patients) showed IUGS by follow up TVS. Second group: (37 patients) had persistent vaginal bleeding and developed acute pelvic pain with or without mild to moderate pelvic collection, or who showed increased B-hCG above the discrimination level (1500 IU) with no IUGS seen in TVS. Patients of this group are subjected to laparoscopic examination with or without dilata-
tion & curettage (D&C). Third group: (10 patients) showed decreased titer of the B-hCG with persistent vaginal bleeding underwent D&C. Fourth group (8 patients): they showed decreased titer of B-hCG and improvement of the vaginal bleeding and abdominal pain. The patients of the fourth group were controlled medically and were excluded from this study.

The final diagnosis of all cases included in this study was made by laparoscopic examination, D&C, or by the appearance of intrauterine gestational sac on follow up by TVS. The findings of the comprehensive TVS were assessed for the previously described six sonographic and color Duplex imaging criteria, and then the approved EPs and CLCs were compared in order to justify the value, sensitivity and specificity of each included sonographic feature.

Results

Seventy three patients were included in this study, 34 patients with approved EP and 39 patients with approved CLC. The quantitative B-hCG was ranging from 723 to 1456 at the time of the comprehensive TVS (mean 950 IU/L; second international standard). The mean maternal age of the patients was 29.4 year ranging from 16-46 years. The mean gestational age according to the last menstrual period was 5 weeks and 5 days ranging from 4 weeks and 1 day to 7 weeks and 3 days at the time of the first TVS.

The hyperechoic cyst wall compared with ovarian parenchyma was significantly more in the EP 91.1% (31 of 34) than in CLC 30.8% (12 of 39). In 47.1% (16 of 34) of EP group the cyst wall was significantly hyperechoic than that of the endometrium compared with the corpus luteum group in which none of the cysts showed hyperechoic wall than the endometrium (Table 1 and 2). The sensitivity, specificity and positive predictive value (PPV) of the hyperechoic cyst wall than the endometrium was 44.1%, 100% and 100% respectively in differentiating EP from CLC. Most of the corpora lutea walls were hypoechoic than the endometrium 89.7% (35 of 39).

The thickness of the cyst wall was significantly greater in the EPs compared with the CLCs. The

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<th>Table 1. Echogenicity of the wall of the cystic structure in comparison with ovarian parenchyma.</th>
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<th>Table 2. Echogenicity of the wall of the cystic structure in comparison with endometrium.</th>
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<th>Table 3. The echo texture of the contents of the cystic structure.</th>
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mean thickness in EPs was 7.1 mm compared to 2.6 mm in CLCs. Thick wall (more than 4 mm) was noted in 85.2% (29 of 34) of EPs and 25.6% (10 of 39) of CLCs.

There was no significant difference in the number of cases showed lacy pattern of the contents of the cyst (table 3). The clear pattern was more in CLCs 58.9% (23 of 39) in comparison to 35.3% (21 of 34) of EPs. The solid/turbid pattern was more common in EPs 50% (17 of 34) than CLCs 23% (9 of 39).

Absent color flow was identified in 3 EP in comparison to 11 in CLCs, whereas mural color vascular flow was found in 91.1% (31 of 34) patients with EP compared to 71.7% (28 of 39) patients with CLC. Yet there was no significant difference in percentage of wall circumference with blood flow between the EP and CLC. 45.1 % of EP showed high flow in comparison to 50% of the CLC.

The RI was measured in the EP and CLC which showed mural blood flow. The RI in EP ranged from 0.18-1.1 mean 0.49 and the RI in CLC ranged from 0.38 - 0.71 mean 0.52. There were no significant statistical differences between the intermediate threshold RIs in EPs and CLCs. However, the difference was significant in the low and high threshold RIs. An RI of less than 0.4 had a specificity and PPV of 100% for diagnosing EP but was seen in only 16.1% (sensitivity) of EPs. However, an RI of greater than 0.7 was present in 32.2% (sensitivity) of EPs with a specificity and PPV of 96.4% and 90% respectively (table 4).

Table 4. The resistive index of the flow in the wall of the cystic structure.

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<td>5</td>
<td>16</td>
<td>10</td>
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<td>16.1%</td>
<td>51%</td>
<td>32.2%</td>
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<td>Corpus luteum</td>
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<td>0%</td>
<td>96.4%</td>
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Fig. 1. Tubal ring echogenicity in relation to the endometrium. A, Ectopic pregnancy in a 32-years-old woman. Endovaginal sonogram shows that the wall of the ectopic pregnancy (EP) is more echogenic than the endometrium. B, another 37-eras-old patient showing the tubal ring of ectopic pregnancy (arrowheads) is more echogenic than the endometrium (End).

Fig. 2. Transverse endovaginal sonogram in an 18-years-old woman shows similar echogenici- ties of the wall of the tubal ring of the ectopic pregnancy (arrowheads) and endometrium (arrow).
Fig. 3. Corpus luteum in a 32-years-old woman. Endovaginal sonogram shows that the wall of the corpus luteum (CLC) is hyperechoic than the ovarian tissue anteriorly and less echogenic than the endometrium (End). Note the clear pattern of the cyst contents.

Fig. 4. Corpus luteum in a 39-years-old woman. Endovaginal sonogram shows clear cystic center, the wall of the corpus luteum (CLC) is less echogenic than the ovarian tissue (Ov) and endometrium (End).

Fig. 5. Ectopic pregnancy compared with corpus luteum cyst in a 37-years-old woman. Endovaginal sonogram shows that the wall of the tubal ring of the ectopic pregnancy (EP) is hyperechoic than the corpus luteum (CLC).

Fig. 6. Transverse endovaginal sonogram in a 42-years-old woman shows the wall of the tubal ring of the ectopic pregnancy (arrows) is more echogenic than the ovary (Ov) and sold pattern of cyst contents.

Fig. 7. A. Complex mass of ectopic pregnancy and corpus luteum, transvaginal sonogram shows a large heterogeneous adnexal mass without distinguishing feature beside the clear corpus luteum cyst in 42 years old women. B, Careful examination of the mass shows an echogenic ring of ectopic pregnancy with turbid contents.
Fig. 8. Tubal ring of ectopic pregnancy in 16 years old woman, transvaginal sonogram with color Doppler examination demonstrates a typical tubal ring (EP) with clear contents and high mural vascular flow pattern.

Fig. 9. Tubal ring of ectopic pregnancy in 24-years-old woman, transvaginal sonogram with color duplex demonstrates a typical tubal ring with low mural vascular flow pattern.

Fig. 10. Corpus luteum cyst in 41-years-old woman, transvaginal sonogram of the left adnexa with color Duplex shows lacy contents of the cyst with high vascular flow pattern.

Fig. 11. Pulsed Doppler interrogation of the mural flow. A, ectopic pregnancy in a 35-year-old woman. Pulsed Doppler interrogation shows a high threshold RI of 0.83.

Fig. 12. Ectopic pregnancy in a 39-year-old woman. Pulsed Doppler interrogation shows an intermediate threshold RI of 0.63.

Fig. 13. Corpus luteum of pregnancy in a 28-year-old woman. Pulsed Doppler interrogation shows an intermediate threshold RI of 0.47.
Discussion

The prevalence of ectopic pregnancy has increased, mostly due to improved detection of EP and the increasing prevalence of fallopian tube disease. The earlier and accurate detection of ectopic pregnancy has been made possible by the combination between quantitative β-hCG and TVS with description and characterization of sonographic components of the adnexal cyst.2,16,19,24-26 Despite the widespread use of TVS for diagnosing EP in the suspected ladies and extensive literature on the subject, there is no consensus regarding the best positivity criterion for the findings differentiating EP from CLC if TVS showed an apparently extra-ovarian cystic adnexal mass other than a simple cyst with absent yolk sac or fetal pole.7-9 The current therapeutic options for EP include expectant management (i.e. close follow-up), medical treatment (usually injections of methotrexate), and surgery. Accurate diagnosis with endovaginal sonography is the prerequisite to nonsurgical management, since surgery is the logical treatment if laparoscopy is used for diagnosis.11,14-15

On TVS the tubal ring sign (an extra uterine sac-like structure) is one of the classic sonographic sings in EPs. It attributes to 40%-68% in Atri14 series, and about 50-71% in Frates et al20 series. On the other hand, the corpus luteum is typically a thick-walled, spherical structure in the ovary, with variable internal contents. Although the ectopic pregnancy is mostly extra-ovarian and the corpus luteum is always intra-ovarian, one of the most common pitfalls is mistaking corpus luteum cyst of pregnancy for EP in the adnexa and vice versa.11,14-15

The tubal ring sign was first mentioned in 1988 by Rottem and Timor-Tritsch.27 Timor-Tritsch 28 reported that the tubal ring is more echogenic than the ovary and more so than CLC. In a group of 88 patients with EPs, Frates et al20 showed the tubal ring was more echogenic than the ovary and more so than CLC. In a group of 88 patients with EPs, Frates et al20 showed the tubal ring was more echogenic than the ovarian parenchyma in 88% of patients. Stein et al22 examined 79 patients for the possibility of EP and CLC and found that the wall of EP was more echogenic than the endometrium in 32% of cases. In our study, most of the tubal ring walls were iso or hyperechoic than the endometrium (figure 1, 2). In 47.1%, the ring wall echogenicity was significantly increased over that of the endometrial echogenicity, a feature that was found in none of the corpora lutea wall. In this cohort, an echogenic wall more than the endometrium had 100% specificity and PPV for diagnosing EP. Conversely, the isoechoic or hypoechoic wall to the ovarian parenchyma had 91.2% and 90% specificity and PPV respectively for diagnosing CLC (figures 3-5). These differences in the echogenicities between tubal ring wall and CLC wall compared with endometrium and ovary can be of a great help in making the diagnosis.

Stein et al22 reported that the only significant predictive internal echo texture feature of the adnexal cystic structure was an anechoic appearance, which was significantly more common in the corpora lutea than in the ectopic pregnancies. They reported that, the lacy, solid, and turbid appearance were not useful for differentiating between EP and CLC. This may be due to the fact that blood may be seen within corpora lutea as well as in ectopic pregnancies, and, depending on the stage of hemorrhage, it may appear as lacy, solid, or homogeneous low-level echoes. In our study, there was no significant difference in the lacy pattern in both groups, however we found that the clear pattern had 65.7% PPV in the CLC group (figure 6, 7) and the solid/cloudy pattern had 65.4% PPV in EP group. In agreement with the Stein et al22 series. In our study, the thickness of the cyst wall was greater in EP (85.2%) compared with CLC (25.6%).

Parsons29 has described that the corpus luteum is the gland “with the highest perfusion per gram of any tissue in the body”. The CLC showed peripheral blood flow seen in 92 to 95%. Whereas the trophoblastic ring of the EP showed blood flow in 85% to 93%, this may be due to the abundant vascularity seen in the periphery of both the tubal ring of an EP and the wall of a CLC.12,22,29-31 In our study 87.2% of CLCs showed peripheral blood flow in comparison to the 91.1% seen in EPs with no significant differences regarding the percentage of the wall circumference with flow between EPs and CLCs (figures 8-10). Although pulsed Duplex interrogation can be used to analyze blood flow within the walls of the corpus luteum,32 there is overlap between the RIs of EPs and CLCs reported in different series.11 Most of the series reported that, RIs is lower in EP, on the other hand, some other series have shown a higher mean RI in EP. The mean resistive index of
EP ranging from 0.36 to 0.61 and the mean RI of the CLC ranged from 0.45 to 0.53. This overlap may be due to the comparison was made in term of mean RI of the overall examined groups. Kurjak et al. suggested RI less than 0.4 to discriminate between EP and CLC. Atri, reported that both extremes of RI discriminated EP from CLC and RI less than 0.39 or greater than 0.7 should help in differentiating EP from CLCs, with specificity and PPV in both values of 100% each. In our study, we classified the RIs into three groups, low, intermediate and high. The intermediate-threshold group (≥ 0.4 to 0.7) showed overlap of the RIs between EPs and CLCs, on the other hand, RI of less than 0.4 (low-threshold RI) had a specificity and PPV of 100% for diagnosing EP and RI of more than 0.7 (high-threshold RI) had a specificity and PPV of 96.4% and 90% respectively for diagnosis of EP (figures 11-13).

**Conclusion**

In conclusion, high resolution transvaginal ultrasound with color Duplex had a valuable role in differentiating ectopic pregnancy from corpus luteum cyst. Many useful sonographic finding are used to differentiate ectopic pregnancy from corpus luteum cyst. The echogenic wall than the endometrium and of course than the ovary, thick wall and low or high-threshold RI of the flow within the wall are all favoring EP with high specificity and PPV. On the other hand, hypoechoic wall than the ovary, thin wall and clear contents of the sac are all favoring corpus luteum cyst.

**References**