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# Assesment of Adnexal Masses by Transvaginal Sonography and Serum CA125 Assay In Pre- And Postmenopausal Women

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**Abstract**

***Objective:*** *To compare the diagnostic accuracy of transvaginal sonography and serum CA125 assay for a clinical diagnosis of malignant nature of adnexal masses.*

***Materials and methods:*** *This prospective study was carried out in the department of Obstetrics and Gynaecology of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, during the period of January 2001 to December 2002. The study included 86 patients scheduled for laparotomy for an adnexal mass. Among them, 56 patients were pre- menopausal and 30 were postmenopausal. Adnexal masses had been diagnosed by bimanual pelvic examination and by both transabdominal and transvaginal sonography before planning surgery.*

***Results:*** *Considering separately the women with benign or malignant masses, the sensitivity and specificity of transvaginal sonography for the diagnosis of malignant ovarian condition in premenopausal women were 80% and 96.08% and in postmenopausal women these were 60% and 80%, positive and negative predictive values in premenopausal women were 66.67% and 98.00%, whereas in postmenopausal women those were 60% and 80%. Therefore the sensitivity, specificity, positive and negative predictive values of transvaginal sonography in premenopausal women were higher than in postmenopausal women. The diagnostic accuracy of transvaginal sonography in premenopausal women was 94.64% and in postmenopausal women was 73.33%. The sensitivity, specificity, positive predictive value and the diagnostic accuracy of serum CA125 for the diagnosis of malignant ovarian condition in postmenopausal women were higher than premenopausal women. But the negative predictive value in premenopausal women was higher 94.87% than in postmenopausal women 88.90%.*

***Conclusion:*** *Transvaginal sonography used alone is the best method for differentiating between benign and malignant adnexal masses with a good diagnostic accuracy in premenopausal women in addition to clinical symptoms and pelvic examination. The good diagnostic accuracy of transvaginal sonography in premenopausal women may suggest that the addition of further test is not warranted. On the contrary in postmenopausal women, lower diagnostic accuracy of transvaginal sonography may require help of further test to improve it.*

***Keyword:*** *Adnexal mass, Transvaginal sonography, Serum CA125.*

## Introduction

It is well known that, if hereditary ovarian cancer families are excluded,incidence of ovarian cancer is significantly higher in postmenopausal than in premenopausal women. On the other hand, ovarian enlargements and both ovarian and tubal masses, are more frequently detected in premenopausal women, because of the ovarian cycle and higher incidence of pelvic inflammatory diseases[1]. Majority of adnexal masses are simple ovarian cysts. In premenopausal women, the differential diagnosis of simple ovarian cysts include functional cyst, parovarian cyst, theca-lutein cyst, polycystic ovary, cystadenomas – both serous and mucinous, cystic teratoma and rarely tubo-ovarian abscess. Simple cyst with haemorrhages may appear as a complex mass which

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also include tubal ectopic pregnancy, endometrioma, pelvic inflammatory disease[2]. There is no follicle or luteal cysts in a postmenopausal ovary, simply because there are no follicles or corpora lutea. The menopausal ovary tends to atrophy and shrinks down when the follicles and ova disappear. Therefore, when such an ovary is palpable, it is not a normal ovary for this stage of life[3]. Solid apparing adnexal masses include subserous pedunculated fibroid, dermoid, thecoma, granulosa cell tumour, brenner tumour, and metastatic ovarian tumour. Tubo-ovarian abscess, ovarian torsion, haemorrhagic cyst and tubal ectopic pregnancy also may appear as solid. Not all the pelvic masses are gynaecological in origin. Pelvic kidney, omental cyst, distended impacted faeces in the rectosigmoid colon, distended bladder, colonic cancer, diverticular abscess and retroperitoneal mass can all be identified by ultrasound as pelvic mass[2].

There is significant correlation between early diagnosis and effective management of an adnexal mass. In the premenopause, the clinician is faced with the dilemma of, on one hand, avoiding unnecessary operations on functional ovarian tumours, such as follicular cysts or corpus luteal cysts and on the other hand, correctly identifying ovarian carcinomas and applying a suitable therapy. The use of reproducible sonomorphologic criteria in combination with a control scan in premenopausal women with ovarian cysts proved to be efficient to reduce the number of unnecessary operations and to evaluate the risk of malignancy[4] . Asymptomatic premenopausal women with simple ovarian cyst less than 5 cm in size can be observed or placed on suppressive therapy with oral contraceptive pill. Surgical intervention will be required if a mass is more than 5cm and contains irregular solid components or is associated with more than 20 ml of intraperitoneal fluid[5]. Postmenopausal women with simple ovarian cyst less 3 cm. in diameter may also be followed, provided the serum CA125 level is not elevated and the patient has no signs or symptoms suggestive of malignancy[6]. As the pelvic bimanual examination appears unreliable for the detection and characterization of small adnexal masses and in particular, in early stage ovarian carcinoma, both biochemical and biophysical methods have been used, including serum CA125 assay, transabdominal sonography and transvaginal sonography[7,8,9].

Transvaginal sonography is a quick and inexpensive imaging technique that easily spots cystic structures of the pelvis. If transvaginal sonography could be applied as a diagnostic tool to differentiate between benign and malignant cysts, this would be of greater clinical and socioeconomic importance as well as time saving [10]. CA125 is the most widely used marker for ovarian malignancy which is not an ideal marker. An ideal marker would especially detect a malignancy and would not be present in nonmalignant tissues. Unfortunately, such an ideal tumour marker is not currently available for ovarian tumour. Most tumour markers utilize antigens that are often found in multiple types of malignancies and many of these antigens or their comparable antibodies can be recognized in normal tissues [11].

CA125 is widely distributed on the surface of both healthy and malignant cells of mesothelial origin, including pleural, pericardial, peritoneal and endometrial cells, as well as in normal genital tract and amniotic membrane. Interestingly the molecule is not present on the surface of normal ovarian cells, but is present in 80% of malignant ovarian tissue of non-mucinous origin[12]. So, it has no diagnostic value and is useful for monitoring the course of disease in patients with invasive epithelial ovarian cancer. A CA125 value greater than normal was found to be associated with the presence of residual tumour. Considering the above facts, the present study was designed to evaluate the role of transvaginal sonography and serum CA125 in differentiating benign and malignant adnexal masses in pre- and post-menopausal women. Results of CA125 value and transvaginal sonography were compared with histopathological findings.

**Materials and methods**

This prospective study was carried out in the Department of Obstetrics and Gynaecology of Bangabandhu Sheikh Mujib Medical University, Dhaka during the period of January 2001 to December 2002. Fifty six pre-menopausal and thirty postmenopausal women scheduled for laparotomy for an adnexal mass were recruited after signed written informed consent.

All premenopausal women were studied during the early follicular phase to avoid the luteal changes of the echo pattern. A full bladder transabdominal sonography was carried out in all women to clarify the special relationship between the mass and other pelvic organs. Then a transvaginal sonography was done in empty bladder for imaging in dorsal position with a slight reverse trendelenburg tilt to localize free

fluid in the pouch of Douglas. If the ultrasound findings were equivocal sonography was repeated on the next day after proper gut preparation. The morphology of the mass was explored first, and then the masses were classified as probably physiological, neoplastic or non-neoplastic variety. After identification of the mass, maximal possible enlargement of the ultrasonographic image on the monitor was applied and the mass was examined carefully in all projections. Tumours were evaluated as either benign or suspicious for being malignant depending upon the sonographic findings.

Both standards and patients' samples were incubated together with biotinylated anti –CA125 monoclonal antibody OV-197 (derived from mice) in streptovidin coated microtiter strips. The CA125 in the standards/ samples is adsorbed in the streptovidin-coated microtiter strips by the biotinylated anti-CA125 monoclonal antibody during the incubation. The CA125 concentration of patients samples were then read from the standard curves.

**Results**

Among the 86 patients, 56 were premenopausal and 30 postmenopausal. In the premenopausal group, majority of the patients (51.8%) were aged 31 to 40 years with mean (±SD) age 35.23 ± 6.73 years (range: 22-48 years). In the thirty postmenopausal group, majority (83.3%)were aged between 51 to 60 years with mean (±SD) age 57.27 ± 3.56 years (range: 51-63 years). At randomization the two groups were comparable for their symptoms, findings and investigations. Table I showed the findings of transvaginal sonography. In 28 (50%) premenopausal women, the diameter of the mass was <7 cm. and in 21 (70%) postmenopausal women it was between 7 to 8 cm. According to the presence of locule, level of echogenicity and presence or absence of fluid in cul-de-sac, the masses were categorized into suspected benign and malignant masses.

**Table- I**

*TVS Findings*

| Findings | Premenopause (n = 56) | | Postmenopause (n = 30) | | Total (n-86) | |
|---|---|---|---|---|---|---|
| | No. | (%) | No. | (%) | No. | (%) |
| Diameter of mass (cm) | | | | | | |
| < 7 | 28 | (50.0) | 2 | (6.7) | 30 | (34.9) |
| 7 – 8 | 18 | (32.1) | 21 | (70.0) | 39 | (45.3) |
| > 8 | 10 | (17.9) | 7 | (23.3) | 17 | (19.8) |
| Locules | | | | | | |
| Unilocular | 29 | (51.8) | 14 | (46.7) | 43 | (50.0) |
| Multiocular | 27 | (48.2) | 16 | (53.3) | 43 | (50.0) |
| Echogenicity | | | | | | |
| Anechoic | 26 | (46.4) | 19 | (63.3) | 45 | (52.3) |
| Low level echo | 11 | (19.6) | 0 | | 11 | (12.8) |
| Mixed echo | 14 | (25.0) | 9 | (30.0) | 23 | (26.7) |
| Echodense Shadow | 5 | (8.9) | 2 | (6.7) | 7 | (8.1) |
| Cul-de-sac | | | | | | |
| Free of collection | 51 | (91.1) | 22 | (73.3) | 73 | (84.9) |
| Collection Present | 5 | (8.9) | 8 | (26.7) | 13 | (15.1) |
| Suspected cases according to TVS | | | | | | |
| Malignant | 6 | (10.7) | 10 | (33.3) | 16 | (18.6) |
| Benign | 50 | (89.3) | 20 | (66.7) | 70 | (81.4) |
| Neoplastic | 26 | (62.0) | 17 | (85.0) | 43 | (61.4) |
| Non-neoplastic | 24 | (48.0) | 3 | (15.0) | 27 | (38.6) |

Table II shows serum CA125 levels in the study subjects. In 39 (69.6%) premenopausal and 18 (60%) postmenopausal women, the level was normal. In 17 (30.4%) premenopausal women and in 12 (40%) postmenopausal women, the level was raised. However, statistically the distribution was not significant.

The distribution of histopathological diagnosis had been shown in Table III. As expected, the prevalence of malignancy was significantly higher in postmenopausal than in premenopausal women (33.3% vs 8.9%). Among benign masses, the prevalence of serous cystadenoma was significantly higher in postmenopause than premenopause (33.3% vs 19.6%). Conversely, the prevalence of cystic teratoma was higher in premenopause than postmenopause (8.9% vs 6.7%). Among the malignant masses, both serous and mucinous cystadenocarcinoma were more prevalent in postmenopausal than premenopausal women. Choriocarcinoma of ovary and dysgerminoma were only present in the premenopausal and endometroid carcinoma in the postmenopausal women.

**Table-II**

*Serum CA125 levels in the study subjects*

| Serum CAI 25 | Premenopause (n = 56) | | Postmenopause (n = 30) | | Total (n-86) | |
|---|---|---|---|---|---|---|
| | NO | % | No | % | NO | % |
| Normal | 39 | (69.6) | 18 | (60.0) | 57 | (66.3) |
| Raised | 17 | (30.4) | 12 | (40.0) | 29 | (33.7) |
| Mean ± SD (U/ml) | 39.90 ± 52.70 | | 48.99 ± 39.15 | | | |
| Range (U/ml) | 1.90 - 305.50 | | 15.03 - 210.10 | | | |

$x^2 = 3.226$, df = 1, p = 0.072 (not significant)

**Table–III**

*Histopathological diagnosis*

| Parameters | Premenopause (n = 56) | | Postmenopause (n = 30) | | Total (n-86) | |
|---|---|---|---|---|---|---|
| Mailgnant Masses | NO | % | No | % | NO | % |
| Serous cystadenocarcinoma | 2 | (3.6) | 5 | (16.7) | 7 | (8.1) |
| Mucinous cystadenocarcinoma | 1 | (1.8) | 3 | (10.0) | 4 | (4.7) |
| Ovarian choriocarcinoma | 1 | (1.8) | 0 | 0 | 1 | (1.2) |
| Edometrioid carcinoma | 0 | 0 | 2 | (6.7) | 2 | (2.3) |
| Dysgerminoma | 1 | (1.8) | 0 | 0 | 1 | (1.2) |
| Total | 5 | (8.9) | 10 | (33.3) | 15 | (17.4) |
| Benign masses Ovarian origin Neoplastic | | | | | | |
| Serous cystadenoma | 11 | (19.6) | 10 | (33.3) | 21. | (24.4) |
| Mucinous cystadenoma | 6 | (10.7) | 5 | (16.7) | 11 | (12.8) |
| Mature cystic teratoma | 5 | (8.9) | 2 | (6.7) | 7 | (8.1) |
| Non-neoplastic | | | | | | |
| Endometrioma | 15 | (26.8) | 0 | 0 | 15 | (17.4) |
| Follicular cyst | 2 | (4.6) | 0 | 0 | 2 | (2.3) |
| Tubal origin | | | | | | |
| Inflammatory mass | 4 | (7.1) | 0 | 0 | 4 | (4.7) |
| Chronic ectopic pregnancy | 3 | (5.4) | 0 | 0 | 3 | (3.5) |
| Others | | | | | | |
| Broad ligament leiomyoma | 2 | (3.6) | 0 | 0 | 2 | (2.3) |
| Parovarian cyst | 2 | (3.6) | 3 | (10.0) | 5 | (5.8) |
| Peritoneal inclusion cyst | 1 | (1.8) | 0 | 0 | 1 | (1.2) |
| Total | 51 | (91.1) | 20 | (66.7) | 71 | (82.6) |

Then findings of TVS and serum CA125 levels in the study subjects compared with histopathological findings to differentiate benign and malignant adnexal masses (Table IV ).

**Table- IV**

*Diagnostic findings of adnexal masses*

| Histopathological | No. | (%.) | TVS finding | | | | CAI 25 finding | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Findings | | | No. | (%) | No. | (%) | No. | (%) | No. | (%) |
| **Premenopause** | | | Malignant | | Benign | | Raised | | Normal | |
| Malignant | 5 | (8.9) | 4 | (80.0) | 1 | (20.0) | 3 | (60.0) | 2 | (40.0) |
| Benign | 51 | (91.1) | 2 | (3.9) | 49 | (96.1) | 14 | (27.5) | 37 | (72.5) |
| Postmenopause | | | | | | | | | | |
| Malignant | 10 | (33.3) | 6 | (60.0) | 4 | (40.0) | 8 | (80.0) | 2 | (20.0) |
| Benign | 20 | (66.7) | 4 | (20.0) | 16 | (80.0) | 4 | (20.0) | 16 | (80.0) |

**Table - V**

*Descriptive statistics*

| | | | Predictive value | | |
|---|---|---|---|---|---|
| Parameter | Sensitivity (%) | Specificity (%) | Positive (%) | Negative (%) | Accuracy (%) |
| TVS | | | | | |
| Premenopause | 80.00 | 96.08 | 66.67 | 98.00 | 94.64 |
| Postmenopause | 60.00 | 80.00 | 60.00 | 80.00 | 73.33 |
| CA 125 | | | | | |
| Premenopause | 60.00 | 72.55 | 17.65 | 94.87 | 71.43 |
| Postmenopause | 80.00 | 80.00 | 66.70 | 88.90 | 80.00 |

Considering separately the women with benign or malignant adnexal masses, the sensitivity and specificity of transvaginal sonography for the diagnosis of malignant ovarian condition in premenopausal women were 80% and 96.08% and in postmenopausal women these were 60% and 80%. The positive and negative predictive values for transvaginal sonography in premenopausal women were 66.67% and 98.00%, those in postmenopausal women were 60% and 80%. The sensitivity, specificity, positive and negative predictive values of transvaginal sonography in premenopausal women were higher than in postmenopausal women. The diagnostic accuracy of transvaginal sonography in premenopausal women was 94.64% and in postmenopausal women it was 73.33%. Sensitivity, specificity, positive predictive value and diagnostic accuracy of CA125 for the diagnosis of malignant ovarian condition in postmenopausal women were higher than premenopausal women. But the negative predictive value in premenopausal women was higher 94.87% than in postmenopausal women 88.90%.

**Discussion**

Malignant neoplasms are uncommon in younger women but becomes more frequent with increasing age. In postmenopausal women with adnexal masses, both primary and secondary neoplasms must be considered along with ovarian fibromas and other lesions as diverticular abscesses[6]. In present study adnexal masses are most frequent between the age of 31 to 40 years in premenopausal women (51.8%) and between 51 to 60 years in postmenopausal women (83.3%). Again, the incidence was lower among the oral contraceptive pill users than other methods users women. This is similar to that reported in other studies[11]. In the premenopause use of reproducible sonography in combination with a control scan proved

to be efficient to reduce the number of unnecessary operations and to evaluate the risk of malignancy. This leaves transvaginal sonography as the valid preoperative evaluation parameter which plays an important role in the preoperative diagnosis of adnexal mass. In this study in premenopausal women, the sensitivity of transvaginal sonography was 80% and specificity 96.08%. The sensitivity of 80% was below the range mentioned in previous studies and the specificity of 96% was in the upper range. Whereas, we achieved a sensitivity of 60% and specificity of 80% in postmenopausal women. The positive and negative predictive values and diagnostic accuracy all were within the range reported by previous authors[1314,15,16]. But it was difficult to interpret because of a large difference in case number between the benign and malignant cases which cause a low false positive predictive value and a high false negative predictive value. The diagnostic accuracy was 94.64% in premenopausal women and 73.33% in postmenopausal women. The significant decrease of the diagnostic accuracy in postmenopausal women may depend, at least in part, on the different prevalence of some diseases in two groups. The results of the present study suggest that the evaluation of suspected adnexal masses should rely on different criteria according to the menstrual status. Because values of serum CA125 are frequently elevated in patients with endometrioma, pelvic inflammatory disease, benign neoplasm, parovarian cyst and peritoneal inclusion cysts it is not possible to establish preoperatively the malignant nature of a pelvic mass[17,18]. In present study, to differentiate adnexal masses the serum CA125 had a lower sensitivity than TVS in the premenopausal women (60% versus 80%) but higher in postmenopausal women (80% versus 60%). The specificity of serum CA125 value was lower than TVS in premenopausal women (72.55% versus 96.08%), whereas it was same in postmenopausal women (80% versus 80%). Positive and negative predictive values and the diagnostic accuracy of serum CA125 were lower than TVS in premenopausal women and higher in postmenopausal women . After matching the results of TVS and serum CA125 with histopathological findings it was found that in premenopausal women, TVS suspected malignancy in 80% cases and serum CA125 value raised in 60% cases. One mucinous cystadenocarcinoma was missed by both the methods and also the value of serum CA125 was normal in dysgerminoma. Among 51 benign masses, 2 endometriomas were confused with malignancy by TVS and serum CA125 values were raised in 17 cases. However, the present study suggests that the evaluation of the findings obtained with the two methods cannot be independent of the menopausal status, which is a highly reliable single indicator for malignancy.

**Conclusion and Recommendation**

Transvaginal sonography used alone is the best method for discriminating benign and malignant masses with a good diagnostic accuracy in premenopausal women. On the contrary, in postmenopausal women lower diagnostic accuracy of transvaginal sonography may require help of further test to improve it. If colour Doppler sonography is used as an additional technique with transvaginal sonography ,the sensitivity and specificity of it increases. Colour Doppler sonography in premenopausal patients lead to erroneous assessment of malignancy because of different blood flow velocity in the ovary during the different phases of menstrual cycle. Further studies will be necessary to evaluate the best diagnostic criteria separately for pre- and postmenopausal women.

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