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Utilization of Pelvic Ultrasonography and CA125 Level to Diagnose Uterine Myoma and Adenomyosis

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ABSTRACT

Background: Preoperative diagnosis of adenomyosis and uterine myoma can be aided by pelvic ultrasonography and cancer antigen 125 (CA125). **Objective:** This study aimed to evaluate the usefulness of CA125 level and transvaginal ultrasonography in diagnosis of uterine myoma and adenomyosis and to differentiate both lesion.

Patients and Methods: One hundred patients complaining of abnormal uterine bleeding were included in this study. They were attending the Obstetrics and Gynecology Departments at Zagazig University Hospitals and Al-Ahrar Teaching Hospital for hysterectomy. Transvaginal ultrasonography (TVS) was done for all selected cases to examine the pelvis for detecting any pathology. CA 125 level was measured. Hysterectomy specimens were histopathologically examined. **Results:** The combination of serum CA125 level and TVS showed that it was useful in adenomyosis group as CA125 level increased the accuracy of TVS from 77% to 80.2%, while in myoma group the combination was not useful as CA 125 decreased the accuracy of TVS from 100% to 83.3%. **Conclusion:** Transvaginal ultrasonography is the most sensitive for myoma (100%) & CA125 level is the most specific (77%) for adenomyosis. CA125 level had the highest sensitivity (87.5%) for adenomyosis than transvaginal ultrasonography (80.1%). Combining both TVS and CA125 level increased the accuracy for detection of adenomyosis to 80.2% but decreased it to 83.3% in detection of uterine myoma.

Keywords: Ultrasonography, CA125, Adenomyosis, Uterine myoma.

INTRODUCTION

The most common benign tumour in women of childbearing age is a uterine myoma, often known as a leiomyoma or a fibroid. Their occurrence increases with age, peaking during childbearing years and declining in the years following menopause. By the time they reached age 50, up to 80% of women had a fibroid diagnosed. They account for 39% of all hysterectomies performed each year, making them the most common cause for the procedure [(1)].

Preoperative diagnostic rates of adenomyosis based on clinical signs are poor, ranging from 3% to 26%, which is not surprising given how rarely adenomyosis was recognized before hysterectomy. Even though the prevalence of adenomyosis at the time of hysterectomy varies widely (from 5% to 70%). Menorrhagia, dysmenorrhea, and dyspareunia are all symptoms of uterine myoma or adenomyosis. Premenopausal women are especially vulnerable [(2)]. Due to the difficulty of performing a complete resection of a focused adenomyosis, preoperative differential diagnosis between adenomyosis and myoma is crucial. Inadequate results have been seen from hormone treatment of adenomyosis [(3)].

Cancer antigen 125 is commonly abbreviated as CA-125. Some patients with certain types of cancer, as well as those with benign diseases, have been found to have increased levels of this blood marker. Even in the absence of pelvi-abdominal pathology, the severity of adenomyosis-related uterine enlargement (defined as a uterine volume more than 240 cm^3 or a gestational age of 12 weeks) was associated with an increase in CA125 levels. However, CA125 levels did not increase above normal in women whose uteruses were enlarged due to fibroids. When the clinical signs are benign, a high CA125 result is not cause for alarm [(4)]. Depending on the results, pelvic ultrasonography can be used to make a preoperative diagnosis of adenomyosis and uterine myoma. Adenomyosis can be diagnosed on ultrasound if the uterus is enlarged, there are cystic anechoic spaces or lakes in the myometrium, the uterine wall is thickened, there are linear striations under the endometrium that are echogenic, the echo texture of the myometrium is irregular, and the endometrial/myometrial border is not clear [(5)]. Patient tolerance and cost-effectiveness make pelvic ultrasonography a popular choice, although results depend heavily on the skill of the ultrasonographer and the quality of the equipment [(2)].

Since total resection of adenomyosis is extremely difficult to execute, it is helpful to differentiate between adenomyosis and uterine myoma prior to hysterectomy in order to decide whether medicinal or surgical treatment is warranted [(6)]. It was the goal of this study to evaluate the usefulness of CA125 level and transvaginal ultrasonography in diagnosis of uterine myoma and adenomyosis and to differentiate both lesion.

PATIENTS AND METHODS

One hundred patients complaining of abnormal uterine bleeding were included in this cross-sectional interventional study. The patients were attending the Obstetrics and Gynecology Departments at Zagazig University Hospitals and Al-Ahrar Teaching Hospital for hysterectomy.

The enrolled patients were classified into three different groups: Group 1: 28 patients with no organic

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lesion, **group 2:** 24 patients who had adenomyosis, and **group 3:** 48 patients who had uterine myoma. The confirmation of diagnosis for each patient was based on histopathological examination

Inclusion criteria: Patients complaining of abnormal uterine bleeding not responding to medical treatment prepared for hysterectomy, after excluding possible malignancy, were enrolled in the study.

Exclusion criteria: Patients with extrauterine pelvic pathology as ovarian masses and tubal swellings, patients with suspected malignancy, and patients who have both adenomyosis and uterine myoma.

This is what all of the participants in this research had to go through:

1. **A thorough review of the patient's medical history**, menstrual, obstetric and contraceptive history were taken
2. **Complete general examination.**
3. **Gynecological examination:** Abdomen and pelvic examination (external genitalia, vagina, cervix, bimanual examination.
4. **Preoperative investigations included:**

- **Conventional 2D-transvaginal ultrasonography:** TVS carried out using Voluson 730 Pro V unit, GE Medical System, Zapf, Austria ultrasound machine with 7 MHz frequency 2D transvaginal probe.
- **Detection of CA125:** CA125 levels in the blood were determined using a sandwich-style, one-step immunoradiometric test kit using two mouse monoclonal antibodies specific for separate epitopes on the molecule (Beckman Coulter Inc., Brea, CA). Up to 35 units per milliliter is considered typical for CA 125 **(7).**
- **Standard preoperative blood tests** and laboratory analyses including liver and kidney function tests, blood sugar levels, complete blood counts, clotting times, and platelet counts.

5. **Hysterectomy:** All patients who underwent a hysterectomy had their specimens analysed by a pathologist. Histopathological analysis of the specimen was coupled with data from sonographic results and CA 125 levels.

Ethical consent:

Research Ethics Council at Zagazig University approved the study (ZU-IRB #5341) as long as all participants provided informed consent forms. Ethics guidelines for human experimentation were adhered to by the World Medical Association's Helsinki Declaration.

Statistical analysis

In order to analyze the data acquired, Statistical Package of Social Services version 20 was used to execute it on a computer (SPSS). In order to convey the findings, tables and graphs were employed. The quantitative data were presented in the form of the mean, median, standard deviation, and confidence intervals. The information was presented using qualitative statistics such as frequency and percentage. The student's t test (T) is used to assess the data while dealing with quantitative independent variables. Pearson Chi-Square and Chi-Square for Linear Trend (X^2) were used to assess qualitatively independent data. The significance of P value of 0.05 or less was determined.

RESULTS

No significant difference among groups as regards age or BMI. Obese cases represented 62% of the studied population (Table 1).

Table (1): Demographics among studied groups

Demographicdata	**Group 1 No organic lesion (N=28)**		**Group 2 Adenomyosis (N=24)**		**Group 3myoma (N=48)**		**Test**	**p-value**
	No.	%	No.	%	No.	%		
Age (years)								
Mean ± SD	43.08±2.978		45 ± 3.173		44.34 ± 4.031		1.989*	0.121
Median (Range)	45.5 (40 – 51)		45 (40 – 50)		46 (41 – 51)			(NS)
Marital status								
Single	3	10.71%	1	4.2	2	4.2	1.53‡	0.465
Married	25	89.29%	23	95.8	46	95.8		(NS)
BMI (kg/m^2)								
Mean ± SD	27.04±4.56		31 ± 3.43		30.50 ± 4.18		0.729*	0.468
Median (Range)	27 (20-37)		31 (26 –36.70)		30 .5 (24 – 37)			(NS)
≤30 (kg/m^2)	10	35.71	7	29.17	21	43.75	1.53‡	0.46
>30 (kg/m^2)	18	64.29	17	70.83	27	56.25		(NS)

30% of the studied patients diagnosed as adenomyosis, 48 % diagnosed as uterine myoma and 22% diagnosed as AUB with no organic lesion by TVS. Group 1 represent 28%, group 3 represent 48% and finally group 2 represent 24% by histopathological examination (Table 2).

Table (2): Studied population as regards diagnosis by transvaginal ultrasonography and histopathology

		N	%
TVS diagnosis	Group 1: No organic lesion	**22**	**22.0**
	Group 2: Adenomyosis	**30**	**30.0**
	Group 3: Myoma	**48**	**48.0**
	Total	**100**	**100.0**
		N	**%**
Histopathology	Group 1: No organic lesion	**28**	**28.0**
	Group 2: Adenomyosis	**24**	**24.0**
	Group 3:Myoma	**48**	**48.0**
	Total	**100**	**100.0**

Transvaginal ultrasonographic criteria for adenomyosis was useful in diagnosis of adenomyosis especially subendometrial echogenic linear striations 91.7%, heterogeneous echotexture 87.5% and cystic anechoic spaces 83.3%. In myoma group, 17 patients had a uterine size >12 weeks, intramural myomas were common, 58.3% had multiple myomas and 68.8 % had myoma size ≤ 5 cm. complications less common (Table 3).

Table (3): Transvaginal ultrasonographic findings of Adenomyosis, uterine myoma groups

TVS findings of adenomyosis	**(N=24)**	
	No.	**%**
Uterine size		
≤ 12 weeks	9	37.5%
> 12 weeks	15	62.5%
Cystic anechoic spaces		
Absent	4	16.7%
Present	20	83.3%
Myometrial Anterior- posterior asymmetry		
Absent	9	37.5%
Present	15	62.5%
Subendometrial echogenic linear striations		
Absent	2	8.3%
Present	22	91.7%
Heterogeneous echo texture		
Absent	3	12.5%
Present	21	87.5%
Obscure endometrial/myometrial border		
Absent	7	29.17%
Present	17	70.83%
TVS findings of uterine myoma		
Patients number	48	100%
Uterine size		
≤12 weeks	31	64.6%
> 12 weeks	17	35.4%
localization		
Submucosal	10	20.8%
Intramural	30	75%
Subserosal	8	4.2%
Number of myomas		
Single	20	41.7%
Multiple	28	58.3%
2ry changes		
Calcifications	3	6.3%
Degenerative changes	1	2.1%
Myoma Size		
≤ 5cm	33	68.8%
> 5cm	15	31.2%
FIGO classification		
1	6	12.5%
2	4	8.33%
3	17	35.42%
4	13	27.1%
5	5	10.4%
6	3	6.25%

TVS showed high sensitivity in diagnosis of uterine myoma (100%), than adenomyosis as its sensitivity represented only 80.1% (Table 4 and figures 3, 4,).

Table (4): Validity of Transvaginal ultrasonography in diagnosis of adenomyosis and uterine myoma

TV Ultrasonography	Group 2 Adenomyosis (n=24)	Group 3 Myoma (n=48)	P Value (Chi-Square Ad)
Sensitivity (%)	80.1%	100	0.082
Specificity (%)	66.7%	100	0.008
Positive Predictive Value. (%)	72.4%	100	0.03
Negative Predictive Value. (%)	53.2%	100	0.0001
Accuracy (%)	77.0%	100	0.08

CA 125 level was significantly higher in adenomyosis than myoma, and higher in myoma than group 1 (Table 5).

Table (5): Validity of CA 125 level in diagnosis of the studied groups

		N	Mean	Std. Deviation	Minimum	Maximum	F/ Kruskall Wallis	P
CA_125 Level	Group 1: No organic lesion	28	8.5417	4.06447	4.00	18.00	**19.784**	**0.00 HS**
	Group 2: Adenomyosis	24	38.5241	32.83715	8.00	195.40		
	Group 3: Myoma	48	15.9957	8.41918	6.00	47.10		

CA 125 level had significant correlation with uterine size and number of fibroids. No significant correlation with site of myoma. It was significantly higher with multiple myomas (Table 6).

Table (6): Serum CA 125 level with uterine myoma in correlation with site, number and uterine size

	n	Mean	SD	Kruskall Wallis	Mann Whitney	P
Site						
Submucosal	10	13.52	7.214	2.312		0.0754
Intramural	30	18.321	9.2145			
Subserosal	8	15.24	8.652			
Number						
Single	20	12.87	8.87		3.987	0.00 HS
Multiple	28	21.41	10.84			
Uterine size						
<12 weeks	31	15.2204	6.73072	-3.98		0.00 HS
≥ 12 weeks	17	29.5241	1183715			

CA125 level as a diagnostic marker of uterine myoma had no role with TVS as it decrease its accuracy. CA125 level as a diagnostic marker of adenomyosis had a role with TVS in diagnosis as it increased its accuracy (Table 7 and figures 1 and 2).

Table (7): Validity of TVS and CA125 level in diagnosis of uterine myoma, and adenomyosis

Uterine myoma					
	Sensitivity%	**Specificity%**	**PPV%**	**PPV%**	**Accuracy %**
CA 125 level	77%	75%	84%	65%	76.3%
TVS	100%	100%	100%	100%	100
CA 125 & TVS	77%	100%	88%	65%	83.3%

Adenomyosis					
	Sensitivity%	**Specificity%**	**PPV%**	**NPV%**	**Accuracy**
CA 125 level	87.5%	82.8%	60%	96.7%	84%
TVS	80.1%	66.7%	72.4%	53.2%	77%
CA 125 & TVS	80.1%	82.8%	66.7%	83.3%	80.2%

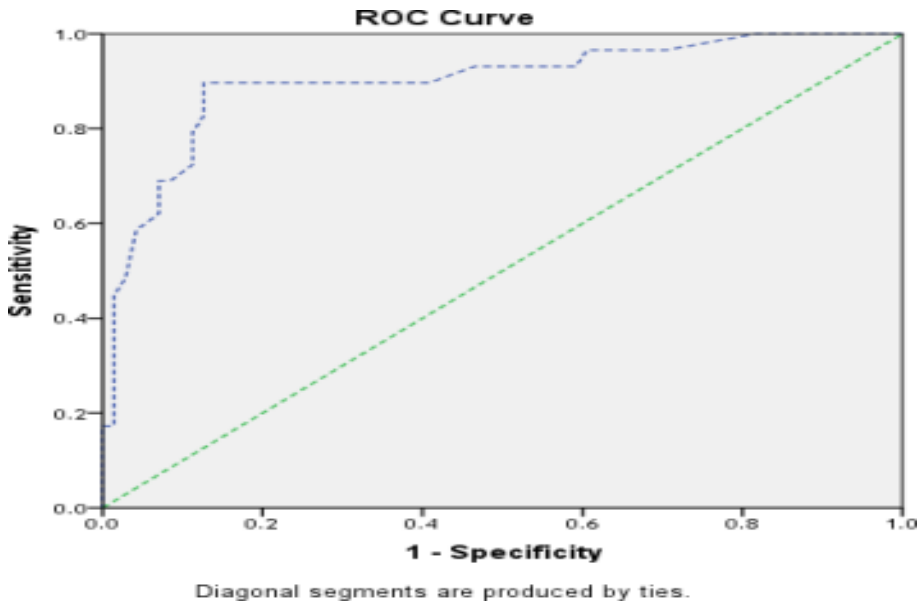

Figure (1): Receiver operating characteristic curve of serum CA125 as a diagnostic marker for uterine myoma.

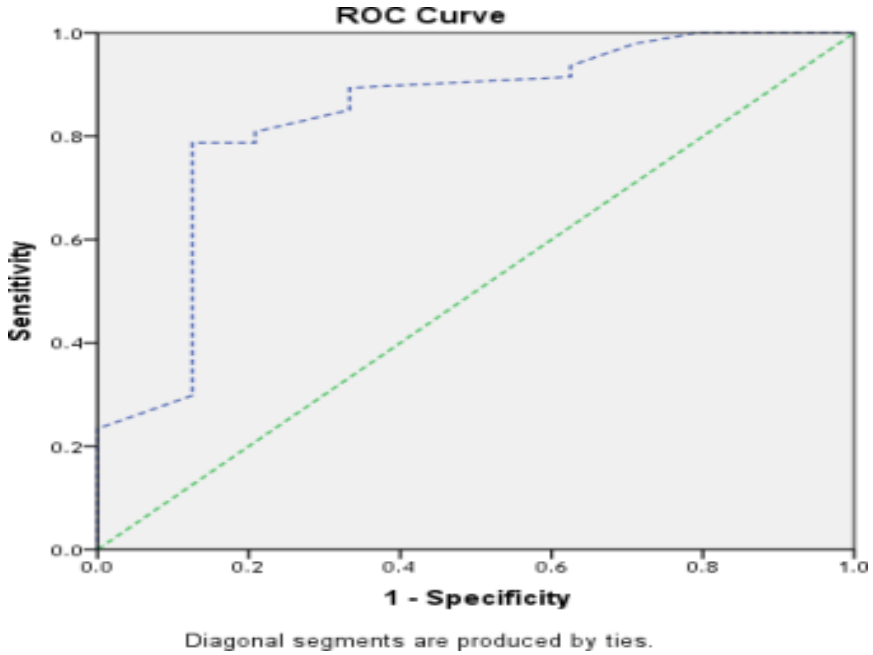

Figure (2): Receiver operating characteristic curve of serum CA125 as a diagnostic marker for adenomyosis.

Figure (3): TVS for a patient showing generalized adenomyosis.

Figure (4): TVS for a patient showing generalized adenomyosis.

Figure (5): TVS of a patient showing intramural fibroid.

DISCUSSION

As regards the demographic data, our results showed that all patients recruited in the study were nearly of the same age group with mean age of 44.17 ± 3.88). 62% of them were obese and 94% were married. There was no significant difference among studied groups regarding age, BMI and marital status. These results go in harmony with **Kil *et al.*** [(2)] and **Puliyathinkal & Surendran** [(8)] as they reported no significant difference regarding age of the studied groups.

According to the ultrasonographic findings of uterine myoma, our results showed that of 48 patients with myoma, 17 patients had enlarged uterus >12 weeks. The patients with intramural myoma represented 75% of the studied group and 28 patients had multiple myomas. 3 patients had calcified myoma and only one had a degenerative changes. 15 patients had myoma size > 5 cm in diameter and the remaining had smaller ones. These results go almost in harmony with **Babacan *et al.*** [(6)] who reported that from 137 patients had myoma, 62 patients had single myoma and 75 had multiple myomas. The patients with intramural myoma represented 65.7% of the studied population. 99 patients had myoma' size ≥ 5 cm.

As regards transvaginal ultrasonography in diagnosis of adenomyosis, our results showed that its sensitivity, specificity, PPV, NPV and accuracy were 80.1%, 66.7%, 72.4%, 53.2% and 77% respectively, suggesting that it is sensitive in the diagnosis of adenomyosis but not specific. These results go in agreement with **Kepkep *et al.*** [(9)] who reported that the sensitivity, specificity, PPV and NPV of TVS in the diagnosis of adenomyosis were 80.8%, 61.4%, 55.3% and 84.4% respectively. Also these results go in harmony with **Hanafi** [(10)] who reported that the sensitivity, specificity, PPV, NPV and accuracy of TVS in the diagnosis of adenomyosis were 84.55%, 43.40%, 75.61%, 57.5% and 71.17% respectively.

As regards TVS in diagnosis of uterine myoma the sensitivity, specificity, PPV, NPV and accuracy were 100%, 100%, 100%, 100%, and 100% respectively. Our results go in agreement, as both were valid, with **Krishnamoorthy** [(11)] who reported that the sensitivity and specificity for TVS diagnosis of myoma were 77.3% & 76% respectively. Also our results go in harmony with **Hanafi** [(10)] who reported

that the sensitivity, specificity, PPVs, NPVs and accuracy of TVS as a diagnostic test for leiomyoma were 96.38%, 96.00%, 99.25%, 82.76% and 96.32% respectively.

As regard CA 125 level in adenomyosis group, with cutoff value of 20.4 U/ml, our results showed 87.5% sensitivity, 82.8% specificity, 60% PPV, 96.7% NPV and 84% accuracy. While, CA 125 level in myoma group, with cut-off value of 10.3 U/ml, our results showed 77% sensitivity, 75% specificity and 84% PPV, 65% NPV and 76.3% accuracy. These results go in harmony with **Kil *et al.*** [(2)] who reported that in adenomyosis group with CA125 cut-off value of 18 U/ml resulted in 74.9% sensitivity, 92.5% specificity and the maximal diagnostic value was 69.3%. While, in myoma group, the cut-off value was 11 U/ml and resulted in 39.4% sensitivity, 71% specificity and the maximal diagnostic value was 28%.

As regard combination of serum CA125 level and TVS, our results showed that it was useful with adenomyosis as CA125 level increased the accuracy of TVS from 77% to 80.2%.while in myoma group the combination was not useful as CA 125 level decreased the accuracy of TVS from 100% to 83.3%.

Our results showed that the differential diagnosis between uterine myoma and adenomyosis using CA125 level could be detected by ROC curve analysis. The results showed that the area under the receiver operating characteristic curve was 0.899 ($P < 0.00$). The CA125 cut-off value for differential diagnosis between adenomyosis and uterine myoma was 20.3 U/ml. Our results are in agreement with **Kil *et al.*** [(2)] who found by ROC analysis that the area under the curve for distinguishing between the adenomyosis group and the myoma group was larger than 0.776, indicating an excellent diagnostic performance (P 0.001). The cutoff value of 19 U/ml for CA125 was used to distinguish between adenomyosis and uterine myoma.

CONCLUSION

We concluded that transvaginal ultrasonography is the most sensitive for myoma (100%) & CA125 level is the most specific (77%). CA125 level had the highest sensitivity (87.5%) for adenomyosis than transvaginal ultrasonography (80.1%). Combining both TVS and CA125 level increasing the accuracy for detection of adenomyosis to 80.2% but decreasing it to 83.3% in detection of uterine myoma.

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