CA125 is not useful in prediction of endometrial adenocarcinoma among post menopausal bleeding

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Abstract

Postmenopausal bleeding (PMB) is vaginal bleeding that happens at least 12 months after your periods have stopped. This study was conducted in Ibb governorate during 2 years to determine the value of serum CA 125 in predicting endometrial adenocarcinoma among postmenopausal bleeding women. The study included 40 PMB women with age range (45-80 years) and mean of 59.9±8.9 years. Diagnosis of the endometrial curettage revealed 8(20.0%) endometrial adenocarcinoma and 19(80.0%) benign endometrial lesions. The mean CA125 was 26.8±19.7 U/mL, it did not show significant difference between PMB due to endometrial adenocarcinoma or other benign endometrial lesions. This study concluded that measuring serum CA125 is not useful in predicting endometrial adenocarcinoma among post menopausal bleeding women and recommended gynecologist to rely only on histopathological diagnosis among PMB women.

Key words:

Postmenopausalbleeding, endometrial adenocarcinoma, CA125, curettage.

الملخص:

النزيف ما بعد إنقطاع الطمث هو النزيف المهبلي الذي يحدث ١٢ شهرا على الأقل بعد إنقطاع الطمث. أجريت هذه الدراسة في محافظة إب خلال عامين لتحديد قيمة المؤشر (CA-125) في مصل الدم للتنبؤ بحدوث سرطان بطانة الرحم بين النساء المصابات بالنزيف بعد سن اليأس. وشملت الدراسة ٤٠ إمرأة مصابة بإنقطاع الطمث من الفئة العمرية (٤٥-٨٠ سنة) بمتوسط ٥٩.٩ ± ٨.٩ سنة.

كشف تشخيص كشط بطانة الرحم أن ٨ (٢٠.٠٪) من النساء مصابة بسرطان بطانة الرحم و ١٩ (٨٠.٠٪) مصابات بآفات حميدة لبطانة الرحم. كان متوسط قيمة المؤشر (CA-125) في مصل الدم ٢٦.٨ ± ١٩.٧ وحدة/مل ولم يظهر فرق كبير بين المصابات بسرطان بطانة الرحم أو غيرها من الآفات الحميدة لبطانة الرحم.

خلصت هذه الدراسة إلى أن قياس المؤشر(CA-125) في المصل ليس مفيداً في التنبؤ بالاصابة بسرطان بطانة الرحم بين النساء المصابات بالنزيف بعد إنقطاع الطمث وأوصت أطباء أمراض النساء بالاعتماد فقط على التشخيص النسيجي لبطانة الرحم.

الكلمات المفتاحية: النزيف بعد إنقطاع الطمث - سرطان بطانة الرحم - CA-125 - الكحت.

Introduction:

Menopause is defined by the World Health Organization as the permanent cessation of menstruation resulting from loss of ovarian follicular activity.(1) Post-menopausal bleeding (PMB) is defined as bleeding that occurs after 1 year of amenorrhea in a woman who is not receiving hormone therapy (HT).(2) PMB is a common problem representing 5% of all gynecologic outpatient attendances.(1)

Endometrial carcinoma is the most common malignancy of the female genital tract in the industrialized countries, it is a common etiology recognized among PBM women.(3)

CA125 (cancer antigen 125 or carbohydrate antigen 125) also known as mucin 16 or MUC16 is a protein encoded in humans by the MUC16 gene. MUC16 is a member of the mucin family glycoproteins. CA125 has found application as a tumor marker or biomarker that may be elevated in the blood of some patients with specific types of cancers, or other benign conditions.(4,5)

CA125 is clinically approved for following the response to treatment and predicting prognosis after treatment. It is especially useful for detecting the recurrence of ovarian cancer.(6,7)

The normal range for CA125 is from 0 to 35 (U/mL). Elevated levels in post-menopausal women are usually an indication that further screening is necessary. In pre-menopausal women, the test is less reliable as values are often elevated due to a number of non-cancerous causes, and values above 35 are not necessarily a cause for concern.(8)

In the study of Dotters, he concluded that measurement of preoperative CA125 is a clinically useful test in endometrial cancer. CA125 levels of >35 U/mL strongly predicted extrauterine disease but lacked sensitivity in identifying patients needing staging.(9)

In this study, the level of serum CA 125 was studied to compare between women who are subsequently diagnosed as endometrial adenocarcinoma and other causes of endometrial postmenopausal bleeding, to determine its value in prediction of endometrial adenocarcinoma.

Method:

This study included 40 female patients with PMB attended to the gynecology clinic of Gebla Governmental Hospital and 2 private gynecology clinics (Al-Kindy hospital and Al-Theqa polyclinic) in Ibb governorate for 2 years (July 2015 - June 2017). Excluding patients with causes of genital bleeding other than uterine causes (cervicitis, cervical trauma, polyp or carcinoma), causes that may raise CA125 such as benign lesions (fibroids or pelvic infections) or malignant lesions (breast cancer or ovarian cancer), and those with history of bleeding disorders or anticoagulants.

All patients in this study were subjected to detailed history taking, thorough clinical examination, 3 ml blood sample from postmenopausal bleeding women prior to fractional curettage taken and sent for estimation of CA125.

A diagnostic technique using endocervical curettage followed by endometrial curettage with two samples examined separately and sent to histopathological examination to assess the type of pathology.

Ethical consideration:

This study took into consideration the most common ethical principles that should be applied to every step of scientific research involving human being. An informed consent was obtained from all patients after providing them a detailed explanation of the objectives, importance and benefits of the study. The relatives were also informed that data will confidentially be handled and used only for research purposes. All patients were followed clinically till the time of hospital discharge and patients diagnosed with endometrial

adenocarcinoma were referred to oncologists for further management.

Statistical analysis:

Data were processed and analyzed by computer facilities using the statistical package of social science (SPSS) program version 24. Quantitative variables included age of the patients and CA125 level were found with parametric distribution, presented as means with standard deviations and tested by the Student T test for the presence of significant difference between 2 means. The statistical tests were conducted with the 95% confidence interval and p-value of > 0.05 was considered statistically insignificant.

Results:

The demographic characteristics of the studied patients with PMB showed that the age ranged from 45 years to 80 years with a mean of 59.9 ± 8.9 years. The commonly affected age groups were 65 – 74 years (37.5%) and 55 – 64 years (32.5%). Most of them were housewives (70.0%) and Illiterates (52.5%) [Table 1].

The histopathological diagnosis of the endometrial curettage revealed that 8 patients were diagnosed as endometrial adenocarcinoma (20.0%), 19 patients with endometrial hyperplasia (47.5%), 11 patients with endometrial polyp (27.5%) and 2 patients with endometrial atrophy (5.0%) [Figure 1].

Serum CA125 in the studied PMB patients ranged from 2.0 to 80.0 U/mL with a mean of 26.8 ± 19.7 U/mL and a median of 23.5 U/mL. The studied patients were grouped as those with endometrial adenocarcinoma (n=8) compared to other benign endometrial lesions (n=32). There is no significant statistical difference between the mean age of PMB patients due to endometrial adenocarcinoma or due to other benign endometrial lesions (p>0.05). Even the comparison of the mean CA125 revealed that no significant statistical difference between both groups (p>0.05) [Table 2].

Discussion:

Post-menopausal blood loss is a common complaint of patients seen in gynecological practice. Women on continuous progesterone and estrogen hormone therapy can expect to have irregular vaginal bleeding, especially for the first 6 months. This bleeding should cease after 1 year. Women on cyclic oestrogen and progesterone should have a regular withdrawal bleeding after stopping the progesterone.[2]

PMB should be considered as due to genital tract malignancy until proved otherwise. Other causes include hormonal replacement therapy, endometria hyperplasia, atrophic endometrium and cervical polyp.[10]

Endometrial cancer is more common in postmenopausal women who are of low parity, obese, diabetic or hypertensive, having estrogen secreting ovarian tumors, on unopposed estrogen replacement therapy or Tamoxifen use for more than 5 years, with family history of breast or ovarian cancer.[11]

Adenocarcinoma represents about 75% of endometrial cancers which originates from the single layer of epithelial cells that line the endometrium and form the endometrial glands.[12]

Vaginal bleeding and/or spotting in postmenopausal women occur in 90% of patients with adenocarcinoma. Also clear white vaginal discharge and/ or lower abdominal pain or pelvic cramping may occur.[13]

In this study, the histopathological diagnosis of the endometrial curettage revealed 8 cases with endometrial adenocarcinoma (20.0%) and the remainder 32 cases were benign endometrial lesions.

The role of CA125 in endometrial cancer was investigated before but the results were conflicting. On assessing serum level of CA125, the studied patients showed higher mean CA125 in those with endometrial adenocarcinoma (34.5 U/mL) than in other endometrial lesions (24.9

U/mL). However, there is no significant statistical difference between the two groups.

This findings is in agreement with the study of Fujimoto et al,[14] who conducted a randomized study on 214 patients with endometrial adenocarcinoma and found that Serum CA 125 level have on significant correlation to the diagnosis. As well as in the study of Zovko et al,[15] among 174 patients with PMB, they did not find significant correlation between CA125 level and histological grade.

Also in the study of Neunteufel and Breitenecker,[16] CA125 was measured by immunohistochemistry in 58 tissue samples of normal epithelia, 21 samples of atypical hyperplasia and 74 samples of endometrial carcinoma, they found that CA125 expression does not correlate with the degree of differentiation of malignancy or atypical hyperplasia.

Additionally, Dotters studied the expression of CA125 by Immunohistochemical tests on 44 patients with histologically confirmed endometrial hyperplasia and 16 patients with histologically confirmed endometrial carcinoma. There was no significant difference in CA125 expression in both atypical adenomatous endometrial hyperplasia and adenocarcinoma. He suggested that CA125 may be of no diagnostic value.[9]

According to the findings of this study, it is suggested that not to rely on CA125 level on predicting malignant from non malignant endometrial lesions.

Conclusion and recommendation:

This study concluded that measuring serum CA125 is not useful in predicting endometrial adenocarcinoma among post menopausal bleeding women and recommended gynecologist to rely only on histopathological diagnosis among PMB women.

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Table.1. Demographic characteristics of the studied patients with post menopausal bleeding

Item	n= 40	
	№.	%
- Age group (years):		
45 – 54	4	10.0
55 – 64	13	32.5
65 – 74	15	37.5
≥ 75	8	20.0
Mean age ± SD	59.9 ± 8.9 years	
- Occupation:		
Housewife	28	70.0
Worker	12	30.0
- Educational level:		
Illiterate	21	52.5
Primary	8	20.0
Secondary	9	22.5
University	2	5.0

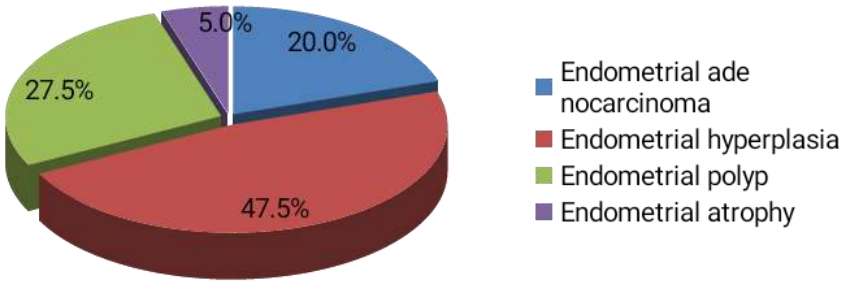

Table.2. Endometrial adenocarcinoma versus other endometrial lesions in post menopausal bleeding			
Item	Endometrial adenocarcinoma (n = 8)	Other endometrial lesions (n= 32)	*p*–value
Mean age (years) Median (Min. – Max.)	61.9 ± 4.9 60.0 (58.0 – 73.0)	59.4 ± 9.6 58.5 (45.0 – 80.0)	0.489*
Mean CA125 (U/mL) Median (Min. – Max.)	34.5 ± 21.5 29.0 (9.0 – 80.0)	24.9 ± 14.1 22.0 (2.0 – 72)	0.221*
**p*–values are statistically insignificant (<0.05)			