RESEARCH ARTICLE

Ovarian Cysts Formation in Patients with Breast Cancer on Tamoxifen Therapy in Iraqi Female

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ABSTRACT

Background: Tamoxifen shows complex hormonal actions, breast cancer that occurs in the premenopausal period treated with tamoxifen created huge quantities of estrogen.

Objectives: This study was conducted to determine the prevalence of ovarian cysts formation in tamoxifen treatments by ultra-sonographic examinations.

Method: A prospective study was carried out in the Oncology and Nuclear medicine specialist Hospital, Mosul/Iraq. There were 14 premenopausal and 36 postmenopausal patients. The inclusion criteria were patients with breast cancer who had been on tamoxifen therapy. Fifty patients were included during a period of 10 months. The following parameters were assessed by ultrasound, endometrial thickness and ovaries conditions, with clinical parameters, age of patients, weight, and associated symptoms.

Results: A total of 50 patients getting tamoxifen management, 14 (28%) of them are premenopausal range their age was between 25 to 44 years, and 36 (72%) postmenopausal range their age was between 45 to 78 years. There's a correlation between the age group of patients and ovarian changes and cystic formation the ovarian cysts were diagnosed. There's a relation between increased endometrial thickness and incidence of ovarian cyst in patients receiving tamoxifen therapy and mild relation between increased endometrial thickness & RT ovarian cystic formation in which the p-value of RT ovary = .049.

In contrast, the LT ovary shows a relation with p-value = .025, which was significant.

Conclusion: Ovarian cysts are common genital tract complications of tamoxifen therapy, which had been developed in this study in about 20% of cases. Ovarian cysts can grow together with premenopausal and postmenopausal patients getting tamoxifen for treated breast cancer.

Keywords: Breast Cancer, Iraqi Female, Ovarian Cysts, Tamoxifen Therapy.

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INTRODUCTION

Tamoxifen shows complex hormonal actions which acts primarily as a non-steroidal anti-estrogenic drug. It also exerts a mild estrogenic effect depending upon the end organ, endogenous estrogen levels, and the tamoxifen dose.[1] It is widely used for the therapy of patients with all stages of estrogen-dependent breast cancer. The single long-term use of tamoxifen has been applied to treat patients during the premenstrual period.[2] On the other side view, it was reported that treatment with tamoxifen as a single agent for estrogen-dependent breast cancer during the premenopausal period is associated with a one- to a three-fold increase of the serum levels of estradiol and progesterone.[3] It was also suggested that tamoxifen potentially stimulates ovarian function accompanied by the formation of persistent follicular functional cysts in premenopausal women.[4,5] Patients take tamoxifen for treated breast cancer to have a high level of estrogen during premenopausal period lead for the growth of ovarian cyst leading to raised E2 levels "Tamoxifen encourages ovarian steroidogenesis in premenopausal females".[6] Tamoxifen interface with granulosa cells, augmenting the FSH driven creation of 17b-E2 lead to arbitrated through its insulin-like growth factor-I action.[7] Tamoxifen management led to incessant ovarian stimulus lead to persistent, bilateral functional ovarian cysts.[8,9] tamoxifen's estrogen-like action on the ovary, Thus the incidence of benign ovarian pathologies in

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breast cancer patients on tamoxifen were found to be higher than that reported for similar pathologies in controls or among non-selected, asymptomatic and untreated women.[10] Ovarian cysts can develop in tamoxifen-treated premenopausal as well as postmenopausal women with breast cancer, Cystic enlargement of an ovary in women with breast cancer can result from functional cysts (in premenopausal women), from metastases of the primary breast cancer or primary ovarian malignancy. It is well known that women with breast cancer have an increased risk of developing ovarian cancer.[11] The purpose of the present prospective study was to follow a group of women with breast cancer on tamoxifen for the occurrence of ovarian cysts by ultra-sonographic examination to assess the factors defining the development of ovarian cysts. Patient features like age, weight, duration of tamoxifen, endometrial thickness, and associated symptoms were evaluated.

METHOD

A prospective study has been done to assess the effect of tamoxifen management on the ovaries of females with breast cancer. The study included 50 patients taken tamoxifen treatment to the Department of radiology from the Oncology and Nuclear medicine specialist Hospital, Mosul, Iraq. This was a cross-sectional observational hospital-based study carried out during the period of February 2018 through November 2018 to survey both ovaries abnormality Data were collected prospectively from Fifty breast cancer patients on tamoxifen. After a breast cancer diagnosis and complete surgical intervention and cytotoxic therapy, a pelvic ultrasound check was done in the hospital after ongoing tamoxifen management. In different periods of consumption of treatment, there were 14 premenopausal and 36 postmenopausal patients; each patient underwent trans abdominal ultrasonography (TAU) with a 1-6 MHz convex transducer (Alpinion Portable Color Doppler E-CUBE). The same physician performed all these examinations. In both ovarian conditions, Ovarian cysts are recognized in the ovary with a diameter of >20 mm in the postmenopausal and >25 mm in the premenopausal patient. Endometrial width, uterus skimmed in the longitudinal flat. The double-layer endometrial width measured at the broadest point between the endometrial-myometrium boundaries in the sagittal plane measured the ovarian presence size. A day-to-day dose of 10 to 40 mg tamoxifen is recommended for each patient. Inclusion criteria: patients with breast cancer who had been on tamoxifen therapy. *Exclusion criteria:* Women with a history of hysterectomy, history of endometrial ablation or hormone replacement therapy during the past 6 months, other known primary malignancy, endometrial sampling during the past 6 months were excluded from the survey. Descriptive statistics are expressed as Pearson Chi-square was used in the case of discrete variables. All the findings of the cases studied were tabulated using Microsoft Excel hence statistical analysis was done by using Statistical packages SPSS18. Paired t-test was used to compare intergroup data. For the evaluation of statistical significance, Chi-square test was employed. Probability values less than 0.05 were considered significant.

RESULTS

A total of 50 patients getting tamoxifen treatment involved, 14 (28%) of premenopausal patients with age range 25 to 44 years, and 36 (72%) postmenopausal with age range 45 to 78 years. At the time when they were monitored for ovarian assessment with relation with other changes of uterus post tamoxifen therapy. The duration of tamoxifen therapy was (range > 6–72) months. In this study, we found a relation between the duration of tamoxifen therapy taken and the incidence of ovarian cyst with RT ovary. It shows 47 (94%) normal-looking by pelvic ultrasound study with 1 (2%) complaining with simple cyst showing measurements' about (52*44 mm), and 2 (4%) cases had complex cysts, with one multiloculated thin wall cyst about (76*63mm), other one thick wall about 2mm with fine echogenic debris within about (30*20.6 mm). On LT ovary shows that 43 (86%) cases had normal ultrasonographic study and 6 (12%) cases had simple cysts, and 1 (2%) case had complaining from a complex cyst. The result shows an increasing incidence of ovarian cysts on both sides in the different ratios in relation to the duration of receiving tamoxifen, the result shows significant relation, with p-value was 0.021. of RT ovary and 0.033 of LT ovary, as shown in Tables 1 and 2. There's a correlation among age group of patients, ovarian changes, and cystic formation that measured by ultrasonography study. The present study covers which ovarian cysts were diagnosed in 10 (20%) patients, 8 of these were premenopausal (57.2%) from the premenopausal patients, which were 14 patients (28%), and 2 were postmenopausal (5.6%) of the postmenopausal subgroup which was 36 patients (72%).

Table 1: Relation between the duration of tamoxifen and RT Ovarian cysts

Duration in months	*Normal*	*Simple cyst*	*Complex cyst*	*Total*	*p-value*
6>	5	0	1	6 (12%)	
6-12	15	0	1	16 (32%)	
13-24	7	0	0	7(14%)	0.021
25-36	6	0	0	6 (12%)	
37-48	7	0	0	7 (14%)	
49-60	4	0	0	4 (8%)	
61-72	3	1	0	4 (8%)	
total	47 (94%)	1 (2%)	2 (4%)	50	

p-value ≤ 0.05 (significant).

The premenopausal patients had 3 cases complaining of ovarian cysts on RT ovary in which 2 of them were complex cysts with a thick wall containing septation measuring 24.6*19.6 mm. The other is a multiloculated complex cyst with 5cystic locules in number measuring 73*62 mm, the last case contained 2 simple cysts measuring 31*21 mm & 52*44 mm respectively with thin wall. The premenopausal patients had 5 cases complaining from ovarian cysts on the LT ovary, in which 4of them simple cysts thin wall measuring 32*42.2 mm, 36*23.8 mm, 25.4*20 and 25.2*18 mm, respectively, last case complaining from the complex cyst with thick wall with fine septation measuring 30*27 mm. In postmenopausal patients were 2 cases complaining from LT ovarian cysts with no patients complaining from RT ovary pathology, the cases were in LT ovary complaining only from simple cysts type which measuring one of the cases had two simple cysts measuring 30.7*36.3 and 46.8*40 mm respectively, other case LT ovary had two simple cysts measuring 47*33.4 mm and 30*29.4 mm, respectively (Table 3 and 4). There is a relation between ovarian cysts in both ovaries. Associated symptoms including abdominal pain, vaginal bleeding, and vaginal secretion, with the relation between the incidence of RT ovarian cysts and relation with associated symptoms, shows high significant relation with PV =0.004. In contrast, the relation between the incidence of LT ovarian cyst & associated symptoms shows P V = 0.027, as shown in Tables 5 and 6.

DISCUSSION

In this study, We noticed that 10 (20%) of 50 tamoxifen-treated female patients complained about ovarian cysts, which shows relation with patients' age and incidence of ovarian cysts. These agree with other results that tamoxifen has a side effect on females in the premenopausal period leading to cyst formation.[5] This agrees with this study in which 8 (57.2%) of 14 (28%) tamoxifen-treated, premenopausal patients had ovarian cysts falling in the premenopausal range. Their age was between 25 to 44 years; also, these results agree with Jale Metindir *et al*. 2005,[12] showing patients with ovarian cysts were younger and more common in premenopausal patients with p = < 0.001. Most of the patients treated with tamoxifen have ovarian cysts in 19 months of treatment. In this study, out of 36 (72%) postmenopausal women, two patients (5.6%) had cystic ovarian formation. Out of 36 patients (72%), with an age range between 45 to 78 years, two cases were from LT ovary complaining about simple cysts type, which measuring one of the cases had two simple cysts measuring 30.7*36.3 and 46.8*40 mm, respectively. In other cases, LT ovary had two simple cysts measuring 47*33.4mm and 30*29.4 mm, respectively, this agreement with The study (Cohen *et al*., 2003)[13] shows 32 (14%) of 332 postmenopausal women with breast cancer who were treated with tamoxifen had simple ovarian cysts. The present study shows an increased incidence of ovarian cysts in both sides with a different ratio considering

Table 2: Relation between the duration of tamoxifen and LT Ovarian cysts.

Duration in months	*Normal*	*Simple cyst*	*Complex cyst*	*Total*	*p-value*
6>	5	1	0	6 (12%)	
6–12	13	2	1	16 (32%)	
13–24	7	0	0	7 (14%)	
25–36	5	1	0	6 (12%)	0.033
37–48	7	0	0	7 (14%)	
49–60	3	1	0	4 (8%)	
61–72	3	1	0	4 (8%)	
total	43 (86%)	6 (12%)	1 (2%)	50	

p-value ≤0.05 (significant).

Table 3: Relation between the age group of patients and RT Ovarian cysts.

	RT ovary				
Age-group	*Normal*	*Simple cyst*	*Complex cyst*	*Total*	*PV*
premenopause	11	1	2	14 (28%)	0.017
Postmenopause	36	0	0	36 (72%)	
Total	47(94%)	1(2%)	2(4%)	50	

p-value ≤0.05 (significant).

Table 4: Relation between the age group of patients and LT Ovarian cysts.

	RT ovary				
Age-group	*Normal*	*Simple cyst*	*Complex cyst*	*Total*	*PV*
Premenopause	9	4	1	14 (28%)	0.018
Postmenopause	34	2	0	36 (72%)	
Total	43 (86%)	6 (12%)	1 (2%)	50	

p-value ≤0.05 (significant).

Table 5: Relation between the incidence of RT ovarian cysts and associated symptoms.

	Ovary-RT				
Associated symptom	*Normal*	*Simple cysts*	*Complex cysts*	*Total*	*P-value*
asymptomatic	37	0	1	38 (76%)	
Abdominal pain	5	0	1	6 (12%)	0.004
Vaginal bleeding	2	1	0	3 (6%)	
Vaginal secretion	3	0	0	3 (6%)	
Total	47 (94%)	1 (2%)	2 (4%)	50	

p-value ≤0.05 (significant).

Table 6: Relation between the incidence of LT ovarian cysts and associated symptoms

	Ovary-RT				
Associated symptom	*Normal*	*Simple cysts*	*Complex cysts*	*Total*	*p-value*
asymptomatic	34	3	1	38 (76%)	
Abdominal pain	4	2	0	6 (12%)	0.027
Vaginal bleeding	2	1	0	3 (6%)	
Vaginal secretion	3	0	0	3 (6%)	
Total	43(86%)	6 (12%)	1 (2%)	50	

p-value ≤0.05 (significant).

the increased duration of receiving tamoxifen therapy. The result shows a significant relation, with p = 0.021. of RT ovary and PV = 0.033 of LT ovary concerning the duration with tamoxifen therapy, this agrees with (Malihe Hasanzadeh *et al*. 2010).[14] In this study, we found a relation between endometrial thickness and incidence of ovarian cysts in patients receiving tamoxifen therapy, which shows increased incidence of ovarian cysts in connection with increased endometrial thickness of patients receiving tamoxifen treatments, which measured by U/S. It shows a mild relation between endometrial thickness and RT ovarian cystic formation in which the p-value of RT ovary = 0.049 while LT ovary p = 0.025, which shows significant relation. This agrees with (Shushan *et al*. 1996),[15] in which investigated the incidence of cystic ovarian formation among tamoxifen-treated breast cancer patients. In premenopausal women, tamoxifen stimulates the ovaries to synthesize estrogens and thus greatly increases the level of plasma estrogen.[16] In postmenopausal females, tamoxifen somewhat decreases plasma estrogen and often elevates serum hormone-binding globulin. This lead to decrease the level of free estradiol.[16] The association between increased body weight of patients and ovarian cysts formation leads to estrogen stimulation remaining developed aromatase activity in the fatty tissue.[17]

CONCLUSION

Ovarian cysts are common genital tract complications of tamoxifen therapy, developed in this study, about 20% of cases. Ovarian cysts can grow together with premenopausal and postmenopausal patients getting tamoxifen for treated breast cancer.

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