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Gynecological Side Effects of Tamoxifen among Sudanese Women, Khartoum, Sudan, 2020

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Abstract

Background: In Sudan, the common endocrine therapy tamoxifen is prescribed to HR-positive patients, which is associated with a variety of complications such as hot flashes, vaginal discharge, and vaginal dryness. **Objective**: This study aimed to determine the gynecological side effects of tamoxifen among Sudanese women who have been diagnosed with breast cancer in Khartoum, Sudan. **Methods**: A retrospective cross-sectional study was conducted at Alzara Hospital in Al Amal Toure Revere, Sudan. A convenience sample of individuals previously diagnosed with breast cancer attended refer clinic. From October 2020 to September 2021, all patients attending were checked for eligibility. **Results**: A total of 100 patients were enrolled in the study; 60% of patients reported increased vaginal secretions after taking the drug, 28% reported normal vaginal secretions with no change, and 11% reported decreased secretions after taking the medication, while 22% developed vaginal bleeding, and 22% of the ultrasound results revealed endometrial masses among the study patients. Also, 54 percent of female patients experienced hot flashes after taking the medication, and 12% of women missed some doses of treatment. **Conclusion**: Tamoxifen results in several gynecological side effects in women with breast cancer. A high percentage of women in the study developed hot flashes, vaginal bleeding, and discharge, in addition to having ultrasound results showing endometrial masses among them.

Keywords

Tamoxifen, Breast Cancer, Gynecological Side Effects, Sudanese Women

1. Introduction

1.1. Background Information

Breast carcinoma is considered the second-most common malignancy in women globally after nonmelanoma skin cancer and causes the majority of cancer mortality in females [1] [2]. Accurate patient management is a critical component of a patient's prognosis. Breast surgery, radiotherapy, and systemic therapies (endocrine therapy, chemotherapy, targeted therapy, and immunotherapy) are among the breast cancer treatment options [3].

Endocrine therapy for breast cancer patients, such as tamoxifen, is regarded as the longest-term treatment received by patients and aims to reduce the incidence of recurrence in a group of patients who are microscopically positive for the estrogen receptor; however, tamoxifen is associated with a variety of gynecological complications, including hot flashes, vaginal discharge, vaginal dryness, and endometrial masses [4] [5].

Due to the lack and high cost of alternative therapies, the majority of Sudanese patients receive conventional therapy due to financial restrictions. Practically no programs exist in Sudan for breast cancer prevention, screening, or early detection. As a result of late-stage disease presentation, patient outcomes are poor.

1.2. Problem Statement and Justification

Due to the dearth of research on the adverse effects of tamoxifen on Sudanese patients, it would allow the health decision-makers to have a baseline of information.

1.3. Objectives

Determining the gynecological side effects of tamoxifen in Sudanese women who have been diagnosed with breast cancer is the aim of this study.

2. Materials and Methods

2.1. Study Design

A retrospective cross-sectional study was conducted in the Sudan from October 2020 to September 2021.

2.2. Study Setting

Alzara Hospital Located in Khartoum State, the capital of Sudan, is considered a specialized oncology hospital and classified as a tertiary-level hospital that provides chemotherapy, radiotherapy, and palliative care. Patients diagnosed with breast cancer are usually referred to Zahra Hospital. The study's sample is therefore representative of the Sudanese population because the hospital is qualified to accommodate patients who come from all over Sudan.

2.3. Participants

Participants in this study were Sudanese women diagnosed with breast cancer (BC) and treated with Tamoxifen. They attended Zahra Hospital for follow-up during the study period. Potential participants were recruited from inpatient wards and outpatient clinics and included only patients who had BC and were treated with tamoxifen.

2.4. Sample

A convenience sample of individuals previously diagnosed with breast cancer attended the clinic and had regular follow-up from October 2020 to September 2021. All patients attending were checked for eligibility and included in the study.

2.5. Selection of Sample and Data Collection

100 female patients were enrolled. In our study, we included patients with breast cancer receiving tamoxifen who were admitted to the Radiation and Isotopes Centre Khartoum (RICK) Hospital and had regular follow-up. We exclude patients who refused to participate, such as patients with breast cancer who don`t take tamoxifen or have irregular follow-up.

Personal information such as age, gender, menopausal status, tamoxifen duration, tamoxifen dose, frequency of medication administration, and tamoxifen side effects (vaginal discharge, vaginal bleeding, character of vaginal discharge, hot flushes, and ultrasound abnormalities) are among the items that were gathered by reviewing medical records in addition to a simple questionnaire designed to confirm required information.

The questionnaire's overall validity coefficient was calculated to be 0.96. In order to identify potential study difficulties and gauge the amount of time needed to complete the questionnaire, five women from different hospitals in Khartoum were randomly chosen to receive the questionnaire as part of a reliability assessment.

The collected data were analyzed using the Statistical Package for Social Sciences, Version 21. Descriptive statistics were used to record the variables; and chi-square analysis was used to assess the relations between the categorical variables. Statistical analysis was carried out, and a p-value equal to or less than 0.05 was considered significant.

2.6. Ethical Approval

Ethical approval was obtained from Omdurman Islamic University, the Ministry of Health in Khartoum State, and the Khartoum Oncology Hospital, and individual consent was taken from each participant before starting the interview.

3. Results

1) Patient characteristics

We enrolled in this study 100 Sudanese women who were diagnosed with

breast cancer; the majority of them were older than 45 years, as their percentage reached 58% of the sample size, while the percentage of those 35 - 45 years was 34% of the sample size, and those aged between 25 and 35 years accounted for 8% of the sample size.

The majority of cases (53%) were classified as menopausal, followed by premenopausal, (38%), and 9% were classified as postmenopausal.

When we asked patients about the duration of taking tamoxifen, we found that the highest percentage was 3 - 5 years, followed by 1 - 2, and the least was more than 5 years: 47%, 43%, and 10%, respectively.

The results showed that 88% of the cases were taking the drug on a regular basis, while 12% the results showed that 88% of the cases were taking the drug on a regular basis, while 12% were not (Table 1).

2) Results of Tamoxifen Side Effects

In terms of vaginal discharge, they increased as the drug was taken; 60% of patients reported increased vaginal secretions after taking the drug, 28% reported normal vaginal secretions with no change, and 11% reported decreased secretions after taking the medication (Figure 1).

When asked if there is vaginal bleeding associated with taking the drug, 70% said no, 22% said yes, but about 8% of the sample size has a different opinion (Table 2).

Table 1. Demographic characteristics of the study population.

Age group	Frequency	Percent
25 - 34 year	8	8.0
35 - 44 years	34	34.0
more than 45	58	58.0
Menopausal status		
Premenopausal	38	38.0
Menopausal	53	53.0
Postmenopausal	**9**	9.0
Duration of taking tamoxifen		
1 - 2 years	43	43.0
3 - 5 years	47	47.0
More than 5	10	10.0
Dose of tamoxifen		
10 mg/twice/day	22	22.0
20 mg/day	78	78.0
Regular treatment		
Regular	88	88.0
Missed some doses	12	12.0

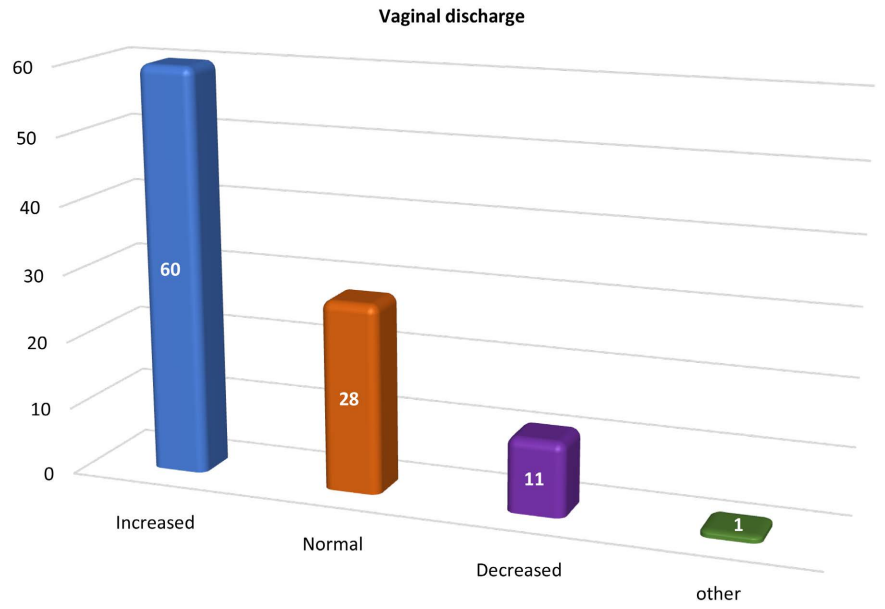

Figure 1. Distribution of the participants according to the vaginal discharge associated with medication.

Table 2. Distribution of the participants according to vaginal bleeding, frequency first time Vaginal bleeding associated with drug.

	Frequency	Percent
Vaginal bleeding		
There is Vaginal bleeding associated with drug	22	22.0
The is no Vaginal bleeding	70	70.0
other	8	8.0

According to the findings, 54 percent of female patients experienced hot flashes after taking the medication, 44 percent did not, and 2% experienced them prior to taking the medication (Figure 2).

We found that 99% of patient files included an ultrasound. 54% of the ultrasounds were done within the last month, while about 45% of the patients had an ultrasound a month ago. 77% of the ultrasounds were normal, while about 22% of the ultrasounds revealed endometrial masses among the study patients (Table 3).

In order to identify the relationship between vaginal bleeding and women's age and menopausal status, "Relationship between the dosage, duration, frequency of administration, and vaginal discharge" and "Association between tamoxifen's gynecological side effects and the dose, duration of taking the medication, and frequency of taking the medication we used cross".

3) Association between tamoxifen side effects in relation to age

The presence of vaginal bleeding was associated with a statistically significant positive relationship (p-value of 0.007), but not with the presence of hot flushes (p-values of 377 and 082, respectively) (Table 4).

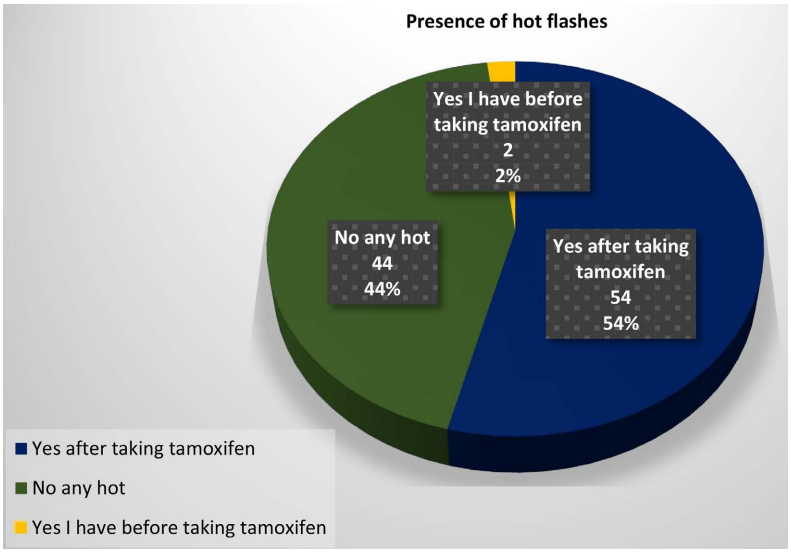

Figure 2. Distribution of patients according to the presence of hot flashes.

Table 3. Distribution of the participants according to ultrasound for one month and it is findings.

	Frequency	Percent
Did you have current vaginal or abdominals ultrasound		
Yes before 1 month	45	45.0
Yes, more than one month before	54	54.0
missing	1	1.0
Ultrasound findings		
Normal	77	77.0
Endometrial mass	22	22.0

Table 4. Association between tamoxifen gynecological side effects and age.

Age groups * Vaginal discharge associated with medication	99	99.0%	1	1.0%	100	0.082
Age groups * Vaginal bleeding	100	100.0%	0	0.0%	100	0.007*
Age groups * Presence of hot flushes	100	100.0%	0	0.0%	100	0.377

4) Association between tamoxifen side effects in relation to, menopausal status

As Table 5 shown there was a statistically significant relationship between vaginal bleeding and patients' menopausal status (p-value of 0.026).

5) Association between vaginal discharge, vaginal bleeding and presence of hot flashes and the dose, duration and frequency of tamoxifen

Our study found that there was a statistically significant relationship between tamoxifen's dose and vaginal discharge (p-values of 0.011), while the results were not significant in relation to vaginal bleeding or the presence of hot flashes (p-values of 0.208 and 0.419, respectively) (Table 6).

Table 5. Association between tamoxifen gynecological side effects and menopausal.

Menopausal status * Vaginal discharge associated with medication	99	99.0%	1	1.0%	100	0.583
Menopausal status * Vaginal bleeding	100	100.0%	0	0.0%	100	0.026*
Menopausal status * Presence of hot flushes	100	100.0%	0	0.0%	100	0.419

Table 6. Association between vaginal discharge & vaginal bleeding and the dose, duration and frequency of tamoxifen.

Dose of tamoxifen? * Vaginal discharge associated with medication	99	99.0%	1	1.0%	100	0.011*
Dose of tamoxifen? * Frequency of Vaginal bleeding	99	99.0%	1	1.0%	100	0.208
Dose of tamoxifen? * Presence of hot flashes	100	100.0%	0	0.0%	100	0.419
Frequency of taking medication * Vaginal discharge associated with medication	99	99.0%	1	1.0%	100	0.024*
Frequency of taking medication * Vaginal bleeding	100	100.0%	0	0.0%	100	0.325
Frequency of taking medication * Presence of hot flushes	100	100.0%	0	0.0%	100	0.008*
For how long did you take tamoxifen * Vaginal discharge associated with medication	100	100.0%	0	0.0%	100	0.028*
For how long did you take tamoxifen * Vaginal bleeding	99	99.0%	1	1.0%	100	0.326
For how long did you take tamoxifen * Presence of hot flashes	98	98.0%	2	2.0%	100	0.227

In addition, our study revealed a significant relationship between the frequency of taking medication and vaginal discharge or the presence of hot flashes (p-values = 0.024, 0.008, respectively) and also significant relationship between tamoxifen duration and vaginal discharge (p-value = 0.028) (**Table 6**).

4. Discussion

The majority of the patients in this retrospective cross-sectional study were menopausal and older than 45 years. Numerous factors are found to cause breast cancer, the most common of which is which are gender, genetic susceptibility, and age [1].

A lack of accurate information and awareness regarding the significance of regular treatment may be the reason why 12% of participants missed some doses when we asked them about regular treatment. There is a need to raise awareness about the importance of treatment adherence among patients who use tamoxifen.

The study showed that women who used tamoxifen developed several gyne-

cological side effects, such as vaginal discharge, vaginal bleeding, hot flashes, and endometrial masses. This is consistent with previous research findings, which revealed that tamoxifen is linked to major complications such as musculoskeletal disorders, fractures, thrombotic events, and endometrial malignancies, ischemic heart disease, arthralgia, headaches, and gynecological complications such as hot flushes, vaginal discharge, irregular bleeding, and sexual problems, as well as endometrial cancer [4] [6] [7] [8] [9].

Regarding vaginal secretions, our study shows 60% of women developed increased vaginal discharge, while 11% experienced a decrease in the secretions after taking tamoxifen.

According to our study findings, there was a statistically significant relationship between the dosage, frequency, and duration of tamoxifen and vaginal discharge. This is due to the fact that Tamoxifen will increase vaginal secretions without actually increasing estrogen levels.

The frequent occurrence of vaginal discharge could be a sign that tamoxifen is effective in converting into more potent metabolites, improving the prognosis for breast cancer. On the other side, dryness in the vagina would suggest that tamoxifen has little estrogenic action on the vagina.

Furthermore, we found that 22% of women who received tamoxifen experienced vaginal bleeding. Because ultrasonography is the most commonly used tool for gynecologic surveillance in tamoxifen-treated BC women in Sudan, our study reviewed the ultrasonography of participating women and showed that 22% of them had endometrial hyperplasia.

The endometrial pathology that we found could be hyperplasia or cancer. Endometrial Pathologies may be more frequent in postmenopausal patients who have received treatment for longer than two years, according to some research [10].

Moreover, our findings provided evidence of an association between that menopausal status and vaginal bleeding; however, tamoxifen use raises the risk of endometrial polyps in all women.

Both before and after menopause, and it has been hypothesized that postmenopausal patients treated for longer than two years have a higher frequency of endometrial polyps [10] and supported by a study that found polyps were the most prevalent endometrial pathology seen in premenopausal breast cancer patients with a history of tamoxifen use [11]; however, the patients in this study did not have endometrial thickness results prior to starting tamoxifen treatment, which is a limitation; additionally, an endometrial biopsy is required to identify the cause of endometrial hyperplasia.

Endometrial abnormalities were found in 61% of women in an Italian study; the abnormalities included benign endometrial polyps 50% of the time, endometrial hyperplasia 10% of the time, and endometrial atrophy 26.3% of the time [12].

As for the 54% of participants who reported experiencing hot flashes, this could be partially explained by the fact that the majority of them are menopausal

women or by the fact that Symptoms may start to manifest when gonadotropin or estrogen levels rise or fall, respectively [13]. This finding agreed with studies that revealed that tamoxifen has known side effects such as hot flashes in 35% of women [14] and [15].

Additionally, we found a significant association between the frequency of medication use and the occurrence of hot flashes. As a result, patients receiving hormonal therapy need to be aware of regular medication use, especially hormonal therapy, as well as regular follow-up and subsequent side effects, such as hot flashes.

5. Conclusions

The study found several gynecological side effects among women diagnosed with breast cancer who used tamoxifen, including vaginal bleeding and discharge and hot flashes. We also found that 12% of them were not on regular treatment.

Reviewed ultrasound results indicate endometrial hyperplasia among the study women.

Our results suggest a positive association between vaginal bleeding and age and menopause; there was also a positive association between the dosage, frequency of taking, and duration of tamoxifen and vaginal discharge.

The study revealed a relationship between hot flashes and tamoxifen use in tamoxifen-treated women that was significantly related to the frequency of tamoxifen use and hot flashes.

Before beginning Tamoxifen treatment, women should be informed about the drug's side effects. In addition, there should be a greater emphasis on compliance, regular follow-up, and regular endometrial thickness testing.

Limitations of the Study

The limitations of this study are the small sample size, as the present study was conducted at the oncology centre. There is a need for future research to examine the knowledge and attitude of Sudanese patients about Tamoxifen treatment in different areas to find out the actual awareness of Tamoxifen treatment among breast cancer patients.

Author Contributions

This work was carried out in collaboration among all authors. Authors YAS and LA designed the study, authors DAHM, SSAM, MAEA and DHAF performed the statistical analysis, and author MAEA wrote the first draft of the manuscript. Authors DRAE and YAS managed the analyses of the study. Authors MAEA, LA and DAHM, managed the literature searches. All authors read and approved the final manuscript.

Conflicts of Interest

The authors declare that they have no competing interests.

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