




# Effect of hormonal therapy on bone mineral density of breast cancer women

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**Website:**

<https://djm.uodiyala.edu.iq/index.php/djm>

**Received:** 29 January 2024

**Accepted:** 8 February 2024

**Published:** 25 April 2024

## Abstract

**Background:** Aromatase inhibitor (AI) was received by breast cancer women with estrogen receptor-positive. The estrogen is the main stimulator for receptor-positive breast cancer cells development and growth, the adjuvant hormone ablation targeting estrogen can decrease the likelihood of cancer recurrence and prolong cancer-free survival.

**Objective:** To determine the effect of this therapy on bone mineral density of women who received it.

**Patients and Methods:** It was identified 100 women with local or regional breast cancer diagnosed and who received AI therapy in the January 2022 to February 2023 from Baqubah teaching hospital/Oncology Centre. It was used DEXA scan to determine the bone minerals density of 50 women after different years from receiving hormonal therapy and other 50 breast cancer women before receiving hormonal therapy.

**Results:** It was shown that there is a significant difference ( $p < 0.0001$ ) in the spine and hip density of breast cancer women who received AIs compare with the bone density of other breast cancer women who did not receive it.

**Conclusion:** It can conclude that AIs plays an essential role for osteoporosis that reduce the quality of health and increase the risk of fraction in the breast cancer women.

**Keywords:** Breast cancer, Hormonal therapy, Bone mineral, Osteoporosis.

## Introduction

Breast cancer (BC) is the most common cancer in women nowadays [1]. However, the mortality rate from BC was declined in last years by the significant advancements in screening programs and therapeutical interventions [2]. Due to increase of women survival after a diagnosis of BC, it was emerged the effect of cancer treatment on the health related quality of life especially its impact on bone health [3,4]. Estrogen stimulate development and growth of breast cancer cells that have receptor-positive and

the adjuvant hormone ablation targeting estrogens could decline the chance for cancer recurrence and prolong survival of cancer patients. In addition, estrogen is an essential bone health regulator and it declines can cause apoptosis of osteocytes, which is the central regulator of bone remodeling and increase osteoclast recruitment that leads to bone loss and osteoporosis in postmenopausal women [5]. Aromatase inhibitors, which are highly effective estrogen suppressors, which are used for the

treatment of ER-positive of early-stage breast cancer in postmenopausal women [6]. However, this treatment induced bone loss that is a common side effect of this therapy. The chemotherapy may increase in bone resorption and aromatase inhibitors decline residual serum endogenous estrogen levels, which lead together to decrease in bone mineral density and increased the risk of fragility fracture [6,7]. Dual-energy X-ray absorptiometry (DEXA) scans is the most important recommended method to measure bone density and determine the osteoporosis by passing a high and low energy x-ray beam via the body in the hip and the spine [8]. Fractures are a significant important cause of morbidity and mortality rates. Moreover, treatment with antiresorptive therapies may inhibit the reduction of bone mineral density of breast cancer women who receive the hormonal therapy [9,10]. Therefore, it is important to do screening for osteoporosis in these patients due to fractures cause health care expenses [4,11]. Accordingly, this study was assessed to evaluate the effect of aromatase inhibitors on bone mineral density of breast cancer postmenopausal women.

### **Patients and Methods**

It was selected 100 women with breast cancer hormonal receptors positive diagnosed in the January 2022 to February 2023 with histologic confirmation that are attended Baqubah teaching hospital/ Oncology Center,

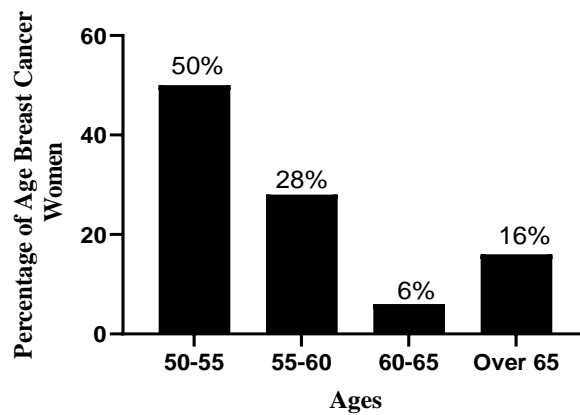
and the age of these women are over 50 years old. DEXA scan was used to determine the bone mineral density of 50 women after received AIs and other 50 women who did not receive hormonal therapy. It was excluded women with hx of osteoporosis and hx of any chronic disease such as thyroid disease, parathyroid disease, celiac disease, DM, asthma, and connective tissues disease. In addition, chronic use of drugs such as thyroid hormones, anticoagulant, diuretics, cyclosporine and steroid that decrease bone mineral density were excluded in this study.

### **Statistical Analysis**

Graphpad Prism software (Graphpad, California, USA) was used for statistical analysis. When appropriate one-way or two-way analysis of variance (ANOVA) was used to compare the groups for studies, and post-test was used to determine statistical significance. The results were expressed as means  $\pm$  standard error of the mean (SEM), significance was defined as (\*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$  and \*\*\*\*  $p < 0.0001$ ).

### **Results**

To determine the bone minerals density of estrogen positive breast cancer women, it was collected 100 breast cancer women. Interestingly, it was found that a high percentage age (50%) of these women was between 50-55 years old and the lowest percentage ages of women (16% and 6%) were over 60 years old Figure (1).



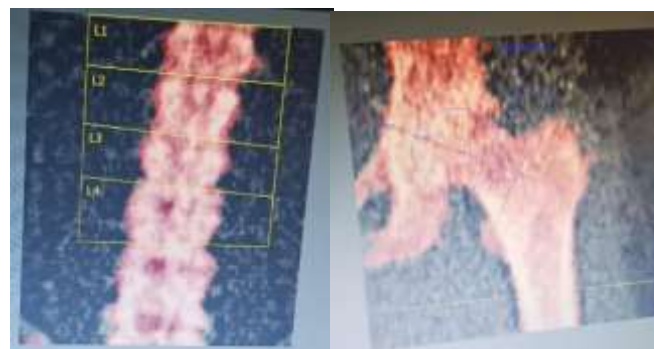
**Figure (1):** Distribution of breast cancer women according to their ages

DEXA scan was used in this study to identify the effect of hormonal therapy (AIs) on bone minerals density. It was showed from the photos in Figure (2, A), there was a clear

osteoporosis of breast cancer women who receiving hormonal treatment compare with normal women in Figure (2, B).



A

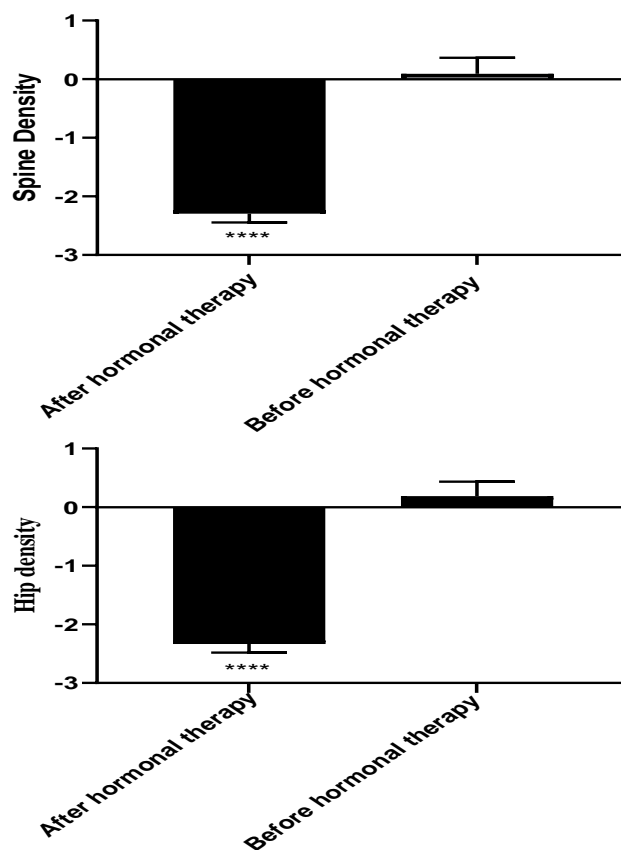


B

**Figure (2):** Photos from DEXA scan of spine and hip of breast cancer women after receiving hormonal therapy (A), and before receiving it (B)

In addition, the results of this study showed that there was a significant difference in the spine and hip density of women who receiving hormonal therapy (-2.29, -2.34,

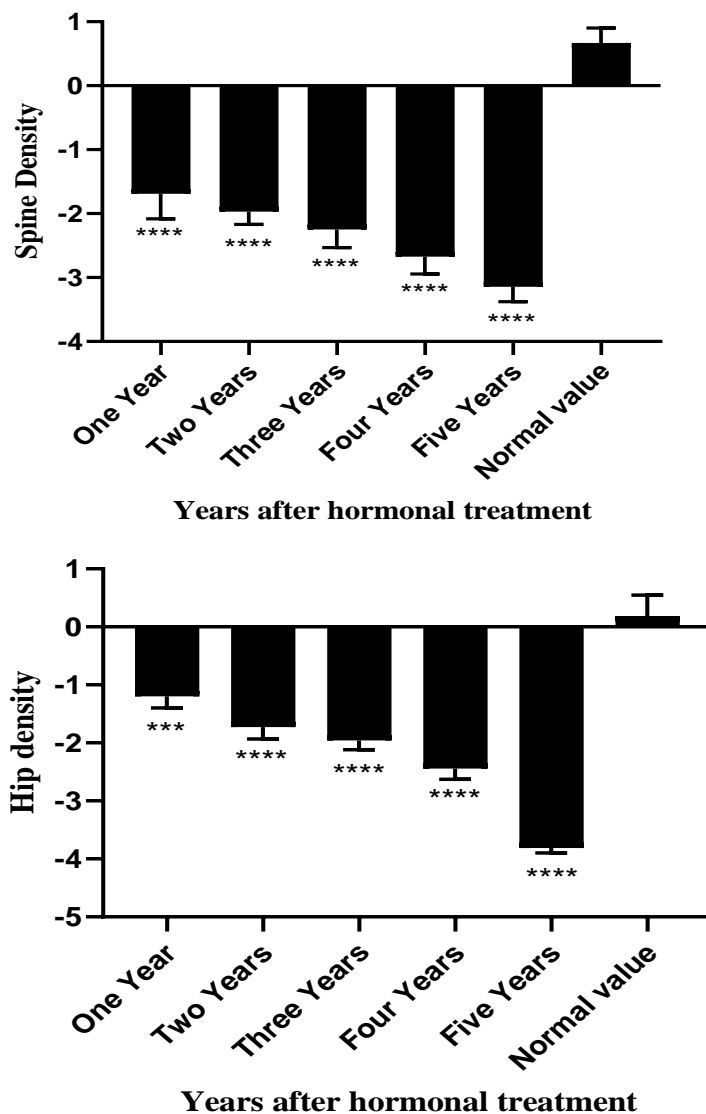
n=50, respectively) compare with the spine and hip density of other breast cancer women who did not receiving AIs (0.092, 0.109, n=50, respectively) (p<0.0001) Figure (3).



**Figure (3):** Spine and Hip density of breast cancer women after and before receiving hormonal therapy. Significant differences were seen by comparing the bone density minerals of women receiving AIs with other women did not receive it (\*\*\*\* p<0.0001)

Having established the effect of the years that the hormonal therapy received by breast cancer women, it was demonstrated that the effect of this therapy on bone minerals density was increased with increasing the duration of receiving it as the spine density was ( -1.69,-1.97,-2.25,-2.68, and -3.14, n=10) after one, two, three, four, and five years, respectively, compare with the spine density of normal value (p<0.0001) (Figure

4). In addition, the hip density was effected by increasing the duration of receiving hormonal therapy as it showed ( -1.2, -1.73, -1.96, -2.4, and -3.81, n=10) in one, two, three, four, and five years, respectively, and there was seen a significant deference between the bone density through these years compare with normal range (p<0001) Figure (4).



**Table (4):** Determination the effect of hormonal therapy on spine and hip density of breast cancer women during the years of receiving it. There was a significant difference in bone density through the years compare with normal value. (\*\*\*)  $p < 0.001$ , (\*\*\*\*)  $p < 0.0001$

### Discussion

In postmenopausal women with hormonal receptor positive breast cancer, AIs are the main important standard adjuvant therapy (13,14). In the other hand, this treatment effects on the health of bone and leads to increase the rate of fractures which may cause disability and death (15-16). Accordingly, the preservation of bone health

is essential in the complex treatment pf women with breast cancer receiving AIs. Therefore, this study was aimed to determine the osteoporosis in the breast cancer women under hormonal therapy to give data for future study and clinical management of survival breast cancer patients.

The age of breast cancer women were selected in the current study were over 50

years old. It was shown that the high percentage age groups that developed breast cancer in women were 50 to 60 years old, and this results similar to the finding of other study which reported that the breast cancer occurred in age between 33 to 60 years old in Iraq [17]. In addition, it was shown that the most breast cancer women (53.8%) were aged 41–55 years in Iraq [18].

In this study, it was found that there is a significant effect of AIs to the bone minerals of breast cancer women who receiving it. Similarly, it was shown that AIs plays a major role for osteoporosis and fracture in women who taken it [19]. In addition, it was reported that AIs prevent cancer recurrence, but it induced bone loss in breast cancer women [20]. Moreover, the finding of this study showed that the consistent decreased in bone minerals of breast cancer women after 3-5 years of AIs administration, and this result agree with other studies that demonstrated the effect of AIs on bone minerals of breast cancer women was increased with prolong duration of administration [21].

In addition, it should be noted that AIs may be taken from (5-10) years [21]. Therefore, it is important to follow up the bone minerals of patients who receiving hormonal therapy and give them replacement treatment when they required [20]. International guidelines recommend the administration of anti-resorptive therapy for all duration of AIs treatment. However, the optimal duration of these therapies is questionable [22,23,24]. On the other hand, it was showed that adjuvant therapy of breast cancer patients should be taken in all postmenopausal women at dangerous for recurrence of cancer [20].

These data suggest that the essential mechanisms of AIs effects on bone minerals in patients with breast cancer need to be more investigated to reduce the risk effect of this therapy on bone health.

## Conclusions

Hormonal therapy (AIs) plays an essential role in osteoporosis in breast cancer women and its effects on bone minerals density, which increase with increasing the years of receiving it. In addition, it was found that the ages between 50 to 55 years old are the high percentage ages of breast cancer women in Diyala city.

## Recommendations

It should be receiving bone health management which consider a cornerstone in the aggregate management of women with estrogen positive who receiving adjuvant AIs. Moreover, it is important to monitor the bone minerals density using DEXA scan during hormonal therapy to reduce the risk of fracture.

**Source of funding:** The current study was funded by our charges with no any other funding sources elsewhere.

**Ethical clearance:** This study was conducted according to the approval of College of Medicine/ University of Diyala and in accordance with the ethical guidelines of the Declaration of ethical committee of the College ( document no.2024AHM824).

**Conflict of interest:** Nil

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## تأثير العلاج الهرموني على كثافة معادن العظام لدى النساء المصابات بسرطان الثدي

علاء حسن مصطفى<sup>١</sup> , حامد عبد إبراهيم<sup>٢</sup> , يسرى جبار حسن<sup>٣</sup>

### الملخص

**خلفية الدراسة:** تم تلقي علاج مثبت الهرمونات (مثبط الاروماتازAI) للنساء المصابات بسرطان الثدي واللاتي يحملن مستقبلات هرمون الاستروجين الايجابية. يعد الاستروجين هو المحفز الرئيسي لتطور ونمو خلايا سرطان الثدي في حالات سرطان الثدي ذو المستقبلات الايجابية، العلاجات الهرمونية التي تستهدف الاستروجين من الممكن ان تقلل احتماليه رجوع السرطان وان تطيل المدة الزمنية للبقاء على قيد الحياة بدون سرطان.

**اهداف الدراسة:** لتحديد تأثير هذا النوع من العلاج على كثافة معادن العظم لدى النساء اللاتي تتلقى هذا النوع من العلاج. **المرضى والطرائق:** تم تحديد ١٠٠ امرأة مصابه بسرطان الثدي ضمن المراحل الثلاث الاولى للورم واللاتي تلقين العلاج الهرموني نوع AI خلال الفترة من شهر كانون الثاني لعام ٢٠٢٢ ولغايه شهر شباط من عام ٢٠٢٣ من مستشفى بعقوبة التعليمي /مركز علاج اورام ديالى. تم استخدام جهاز فحص هشاشه العظام لتحديد كثافه معادن العظام ل ٥٠ امرأة بعد عدة سنوات من تلقيهن العلاج. وعمل فحص الهشاشة ل ٥٠ اخريات قبل تلقيهن العلاج الهرموني.

**النتائج:** تبين من خلال البحث وجود فرق ملحوظ في كثافه العظم في منطقه العامود الفقري ومنطقه الحوض لدى النساء اللاتي تلقين العلاج الهرموني مقارنة باللاتي لم تتلقى العلاج بعد.

**الاستنتاجات:** يمكن الاستنتاج بان العلاج الهرموني AI يلعب دورا اساسياً في الإصابة بهشاشه العظام مما يقلل من جوده الصحة ويزيد من خطر الإصابة بالكسور لدى النساء المصابات بسرطان الثدي.

**الكلمات المفتاحية:** سرطان الثدي, العلاج الهرموني, معادن العظام, هشاشة العظام.

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تاريخ استلام البحث: ٢٩ كانون الثاني ٢٠٢٤

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