

**EVALUATION OF AROMATASE ACTIVITY IN PRE AND POSTMENOPAUSAL  
BREAST CANCER WOMEN**Enas H. Hameed\*<sup>1</sup> Sura Z. Hussein<sup>1</sup> and Nazar A. N. Abed<sup>2</sup><sup>1</sup>Chemistry Department College of Science Tikrit University Iraq.<sup>2</sup>Clinical Biochemistry Unit Tikrit Teaching Hospital Iraq.

\*Corresponding Author: Enas H. Hameed

Chemistry Department College of Science Tikrit University Iraq.

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**ABSTRACT**

Cancer is a group of diseases that cause cells in the body to change and grow out of control. Most types of cancer cells eventually form a lump or mass called a tumor. Breast cancer is the second most common prevalent and diagnosed cancer that affects women and the leading causes of cancer death and disability. Over 30% of all new cancer cases in women are breast cancer worldwide. Aromatase, a catalyzes the conversion of androgens to estrogens in many human tissue sites. The biosynthesis of estrogen plays a principal role in neoplastic formation, especially in women health. For breast cancer, aromatase activity and its inhibition have become a focus of treatment historically. Also, current pharmaceutical agents classified as aromatase inhibitors characterize the importance of this enzyme in steroid biosynthesis due to the potent impact of the estrogen product. Serum samples were collected from 140 women, 50 of these women were control and 90 women were breast cancer patients attending to cancer center in Erbil city from January 2017 to August 2017. Study populations classified into three groups which age ranged from (29-65) years, total subjects, pre and postmenopausal women. The results showed a highly significant decrease ( $P \leq 0.01$ ) in aromatase activity in total and (pre and postmenopausal) breast cancer patients compared to healthy control. Decreased level of aromatase is more common in metastatic breast cancer patients compare to healthy control group.

**KEYWORDS:** Cancer, biosynthesis, women health.**INTRODUCTION**

Breast cancer is the most prevalent cancer among women and affects approximately one million women worldwide each year. It comprises 18% of all female cancers. The breast is made of lobes and ducts, each lobe is made up of lobules, and at the end of the lobules are tiny bulbs that can produce milk. The lobes, lobules and bulbs are connected by tiny tubes called ducts. Each breast has 15 to 20 lobes. Most breast cancers rise in either the lobules or the ducts in the breast. The breast also has lymph vessels which lead to the lymph nodes under the arms.<sup>[1]</sup> Aromatase is a principal enzyme involved in the catalytic conversion of adrenal androgens (testosterone and androstenedione) to aromatic oestrogens (estradiol-E2 and estrone-E1, respectively). In this respect, studies have demonstrated that local production of oestrogen in breast cancer tissue is higher than in normal breast counterparts due to the presence of very high level of aromatase.<sup>[2]</sup> The inhibition of aromatase is a suitable treatment for a number of clinical conditions that are caused or aggravated by the overproduction of estrogen.<sup>[3]</sup>

The aromatase is required for the synthesis of estrogen via aromatization of androgens such as testosterone,

Circulating levels of estrogen decrease as a woman enters menopause, since there is no longer production of estrogen by the ovaries. Thus, the local synthesis of estrogen by breast adipose tissue plays a large role in the growth and survival of ER-positive breast tumors. Inhibition of aromatase activity in these tumors is a rational treatment strategy to suppress estrogen production in peripheral tissues, thus inhibiting tumor growth. The aromatase is localized in the endoplasmic reticulum of estrogen-producing cells.<sup>[4,5]</sup>

Aromatase inhibitors are avoided in women who are premenopausal at diagnosis even if they develop chemotherapy-associated amenorrhea as there are concerns that reduced estrogen feedback to the hypothalamus and pituitary will stimulate gonadotropin release and thus ovarian stimulation.<sup>[6]</sup>

**PATIENTS AND METHODS**

Serum samples were collected from 140 women, 50 of these women were control and 90 women were breast cancer patients attending to cancer center in Erbil city from January 2017 to August 2017. Study populations classified into three groups which age ranged from (29-

65) years, total subjects, pre and postmenopausal women.

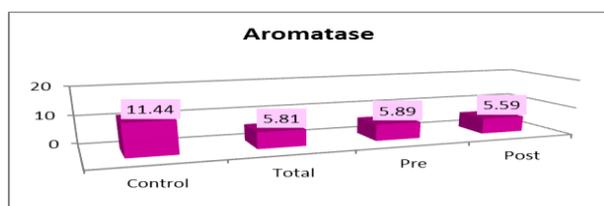
Five milliliters (mls) of venous blood were drawn from each patients and control by vein puncture, left to clot, and then centrifuged at 4000 r.p.m. for 15 min. Serum was separated and stored at -20 C° until time of analysis. The aromatase level was detected by ELISA Kit 96 Tests instrument.

## RESULTS

The mean  $\pm$  SD of serum aromatase level for total breast cancer and healthy control was shown in (table and figure 1) which was (5.81  $\pm$  5.23) ng /ml and (11.44  $\pm$  3.43) ng /ml respectively. These results showed that there was a highly significant decrease ( $P \leq 0.01$ ) in total breast cancer patients compared to healthy control, while the mean  $\pm$  SD of serum aromatase level for Premenopausal and Postmenopausal of breast cancer patients was (5.89  $\pm$  4.85) ng /ml and (5.59  $\pm$  4.34) ng /ml respectively these results showed that there was a highly significant decrease ( $P \leq 0.01$ ) in Premenopausal and Postmenopausal of breast cancer patients compare to healthy control.

**Table 1: Level of Aromatase (ng/ml) in breast cancer women and control.**

Groups	No. of subjects	mean $\pm$ SD	P value
Control	50	11.44 $\pm$ 3.43	
Total	90	5.81 $\pm$ 5.23	$P \leq 0.01$
Premenopausal	50	5.89 $\pm$ 4.85	$P \leq 0.01$
Postmenopausal	40	5.59 $\pm$ 4.34	$P \leq 0.01$



**Figure 1: Level of Aromatase in breast cancer women and control.**

## DISCUSSION

Aromatase inhibitors are essentially useful in postmenopausal patients because they inhibit extra-ovarian aromatase. Because ovaries in premenopausal women can raise estrogen levels by reflex increases in luteinizing hormone (LH) and follicle stimulating hormone (FSH); but in postmenopausal women these main estrogen sources and expression regions are peripheral tissues and estrogen synthesis may be suppressed by aromatase inhibitors. Therapies of postmenopausal hormone-dependent breast cancer patients contain two different strategies: One of them is blocking the connection between estrogens and their receptors by anti-estrogens, other one is inhibition of estrogen synthesis by aromatase inhibitors.<sup>[7]</sup> aromatase

inhibitor is reduce the recurrence risk of cancer.<sup>[8,9]</sup> But as a result of aromatase existing in many other tissues, inhibiting all of them with aromatase inhibitors may cause some side effects like osteoporosis, hot flashes while inhibiting the growing of tumor tissue in breast.<sup>[10]</sup> Therefore aromatase inhibitors, which decrease both aromatase expression and estrogen synthesis, may be optimal agents to prevent breast cancer, clinical trials are going on for this purpose.<sup>[11]</sup>

## CONCLUSIONS

In total, premenopausal, postmenopausal breast cancer patients aromatase level was decreased, in patients compare to healthy control group.

## REFERENCES

- Horton, M. B. Breast Cancer, 2010; 7. <http://www.Google.com>.
- R. J. Santen, H. Brodie, E. R. Simpson, P. K. Siiteri, and A. Brodie, "History of aromatase: saga of an important biological mediator and therapeutic target," Endocrine Reviews, 2009; 30(4): 343–375.
- I. Obiorah, V.C. Jordan, Progress in endocrine approaches to the treatment and prevention of breast cancer, Maturitas, 70: 315–321, <http://dx.doi.org/10.1016/j.maturitas.2011.09.006>.
- C. Stocco, "Tissue physiology and pathology of aromatase," Steroids, 2012; 77(1-2): 27–35.
- G. Di Nardo and G. Gilardi, "Human aromatase: perspectives. in biochemistry and biotechnology," Biotechnology and Applied. Biochemistry, 2013; 60(1): 92–101.
- Chumsri S, Howes T, Bao T, Sabnis G, Brodie A. Aromatase, aromatase inhibitors, and breast cancer. J Steroid Biochem Mol Biol., 2011; 125: 13–22.
- Jelovac D, Macedo L, Goloubeva OG, Handratta V ve Brodie AM. Additive antitumor effect of aromatase inhibitor letrozole and antiestrogen fulvestrant in a postmenopausal breast cancer model. Cancer Res., 2005; 65(12): 5439-5444. (PMID: 15958593).
- Travmergen EN, Levi R, Kamar A ve Travmergen E. Aromataz inhibitorlerinin Yeni Bir Tedavi Seceneđi Olarak Ovulasyon induksiyonunda Kullanılması. Turk Fertilite Dergisi, 2003; 11(1): 21-26.
- Untch M ve Jackisch C. Exemestane in early breast cancer: a review. Ther Clin Risk Manag, 2008; 4(6): 1295–1304. (PMID: 19337436).
- Bulun SE, Chen D, Lu M, Zhao H, Cheng Y, Demura M, Yilmaz B, et al. Aromatase excess in cancers of breast, endometrium and ovary. J Steroid Biochem Mol Biol., 2007; 106(1-5): 81–96. (PMID: 17590327).
- Santen RJ, Brodie H, Simpson ER, Siiteri PK ve Brodie A. History of aromatase: saga of an important biologic mediator and therapeutic target. Endocr Rev., 2009; 30(4): 343-375. (PMID: 19389994).