

Clinical Study of the Serotonin, Melatonin, Estradiol, and Adiponectin Hormones in Women with Breast Cancer in Thi – Qar Governorate - Iraq

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ABSTRACT

Objective: Breast cancer is the most widely cancer among women, involving 18% of all female cancers, and worldwide, breast cancer is the fifth most common cause of cancer mortality. The study was designed to determine and compare the levels of Serotonin (ST), Melatonin (MT), Estradiol (E2), and Adiponectin (ADP) Hormones in Breast cancer patients and apparently healthy individuals. Material and Methods: Blood Serotonin (ST), Melatonin (MT), Estradiol(E2), and Adiponectin (ADP) Hormones levels were determined in 85 Breast cancer patients and 55 apparently healthy subjects. Results: The levels of serum Serotonin (ST), Melatonin (MT), and Adiponectin (ADP) Hormones were showing significant decrease in Breast cancer patients as compared to control group. ($P \leq 0.05$). While the level of serum Estradiol (E2) was showing significant increase in Breast cancer patients as compared to control group.($P \leq 0.05$). Conclusion: In Breast cancer patients, we finding decrease in Serotonin (ST), Melatonin (MT), and Adiponectin (ADP) Hormones. While we finding increase in Estradiol (E2) in Breast cancer patients as compared to control group.

Keywords: Breast cancer, Serotonin, Melatonin, Estradiol, and Adiponectin Hormones.

INTRODUCTION

Breast cancer is the most widely cancer among women, involving 18% of all female cancers, and worldwide, breast cancer is the fifth most common cause of cancer mortality (Bray *et al.*, 2012).

According to a recent report published by the American Cancer Society, breast cancer is the most common type of cancer in women, in the USA. In 2017 alone, studies indicate that approximately 252,000 new cases of invasive breast cancer and 63,000 cases of in situ breast cancer are expected to be diagnosed, with 40,000 breast cancer-related deaths expected to occur (DeSantis *et al.*, 2017).

Serotonin exhibits a growth stimulatory effect on several types of carcinoma, carcinoid and other tumor cells, conversely few data are available on serotonin association in cancer cell migration and metastatic processes, serum serotonin level was observed to be suitable for prognosis evaluation of urothelial carcinoma in the urinary bladder, adenocarcinoma of the prostate and renal cell carcinoma, it really utilized in oncology as tumor marker of gastrointestinal carcinoid, hepatic and ovarian carcinoid (Sarrouilhe D. *et al.* , 2015). In mammals, serotonin is biosynthetically derived by two enzymatic steps: (1) ring hydroxylation of the essential amino acid tryptophan by tryptophan hydroxylase, the rate-limiting step, and (2) side chain decarboxylation by aromatic amino acid decarboxylase (Nichols D. and Nichols C. , 2008, Pytliak

M. *et al.*, 2011, Chojnacki C. *et al.* ,2013, Sarrouilhe D. *et al.* , 2015).

Melatonin interferes with cancer at all the phases of the illness: initiation, progression and spreading from the primary focus, surprisingly, many molecular mechanisms have been proposed to clarify its inhibitory actions (Reiter R. *et al.*, 2017). At first, most of the studies addressing the oncostatic activities of melatonin were performed in animal models undergoing chemically-induced mammary tumors and also in estrogen responsive human breast cancer cell lines.(Cos S. *et al.*, 2014).

About 70% of all breast cancers express estrogen-receptors (ER+) and circulating concentrations of estrogens are positively connected with an increased risk of BC in premenopausal women (Key T. *et al.* ,2013).

The particular role of estrogens in the physiopathology of breast cancer explains why chemoprevention utilizing any drug able to antagonize their actions would be taken into consideration (Costa M. and Saldanha, P., 2017).

Low blood concentrations of adiponectin are related with high incidence and poor prognosis of breast cancer (Fu Y. *et al.*, 2005, Stumvoll M., 2002). Adipose tissue serves as the site of periphegbral aromatization of adrenal androgens to estrogens, which induce mitogenic activity in mammary tissue by binding to estrogen receptors, a diponectin has been inversely associated with estrogen levels, remains possible that adiponectin may influence breast cancer risk

Table 1: Serum Serotonin concentrations of (control) and (breast cancer) groups.

Group	n	Serotonin concentrations (ng/mL) mean± SD
control	55	51.29±14.76 ^a
Breast cancer	85	11.84±2.17 ^b
LSD		2.17

* Each value represents mean ± SD values with non-identical superscript (a , b or c ...etc.) were considered significantly differences (P ≤ 0.05).

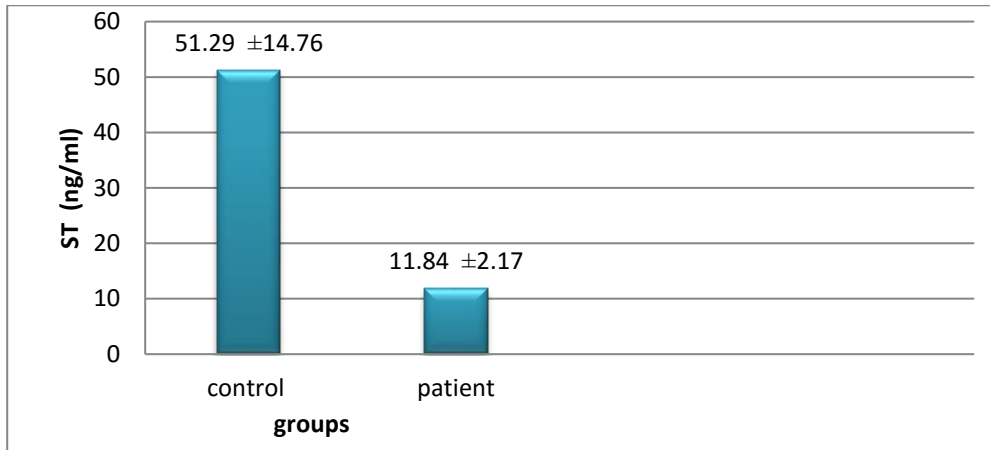


Figure 1: Serum ST levels of control and breast cancer women groups.

Table 2: Serum Melatonin concentrations of (control) and (breast cancer) groups.

Group	n	Melatonin concentrations (pg/ mL) mean ± SD
control	55	22.71±4.13 ^a
Breast cancer	85	10.72±2.29 ^b
LSD		0.83

- Legend as in table (1)

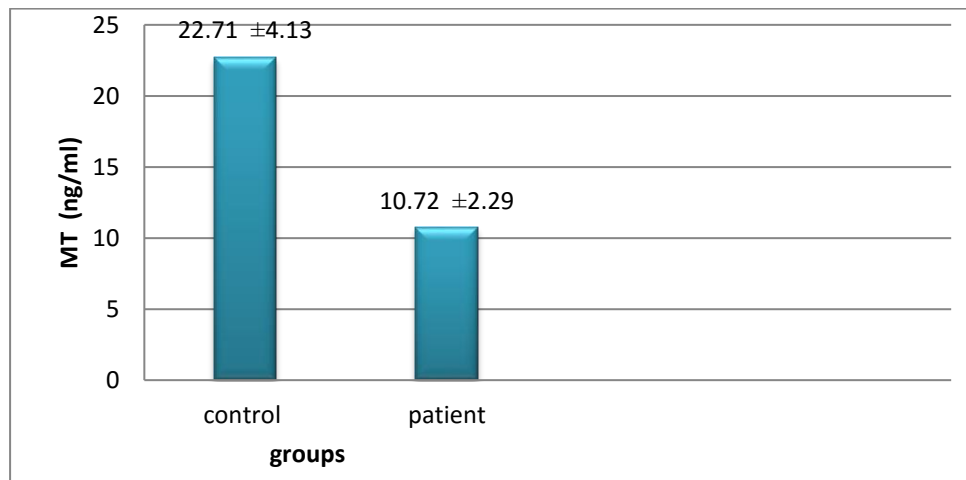


Figure 2: Serum MT levels of control and breast cancer women groups.

by altering circulating estrogen levels (Nabablou M. *et al.*, 2014).

MATERIAL AND METHODS

This study designs as prospective study, all samples are taken from patients who attended the oncology unite in Al-Habooby Hospital and specialist clinics. including (85) blood samples from patients with breast cancer, (55) blood samples are collected from healthy women as a control group.

A bout (5mL) of blood samples of breast caner patients and controls were taken and allowed to clot at room temperature in empty disposable tubes centrifuge to separate it in the centrifuge at 3000 rotor per minute (rpm)for 10min, the serum samples were separated and stored at (-20°C) until analyzed for Serotonin, Melatonin, Estradiol, and Adiponectin hormones.

Serum Serotonin, Melatonin, Estradiol, and Adiponectin hormones were estimated by enzyme linked immunoassay method by ELISA Reader, USA using kit supplied by

Table 3: Serum Estradiol concentrations of (control) and (breast cancer) groups.

Group	n	Estradiol concentrations (pg/ mL) mean \pm SD
control	55	113.84 \pm 14.53 ^b
Breast cancer	85	1581.79 \pm 2.29 ^a
LSD		6.33

- Legend as in table (1)

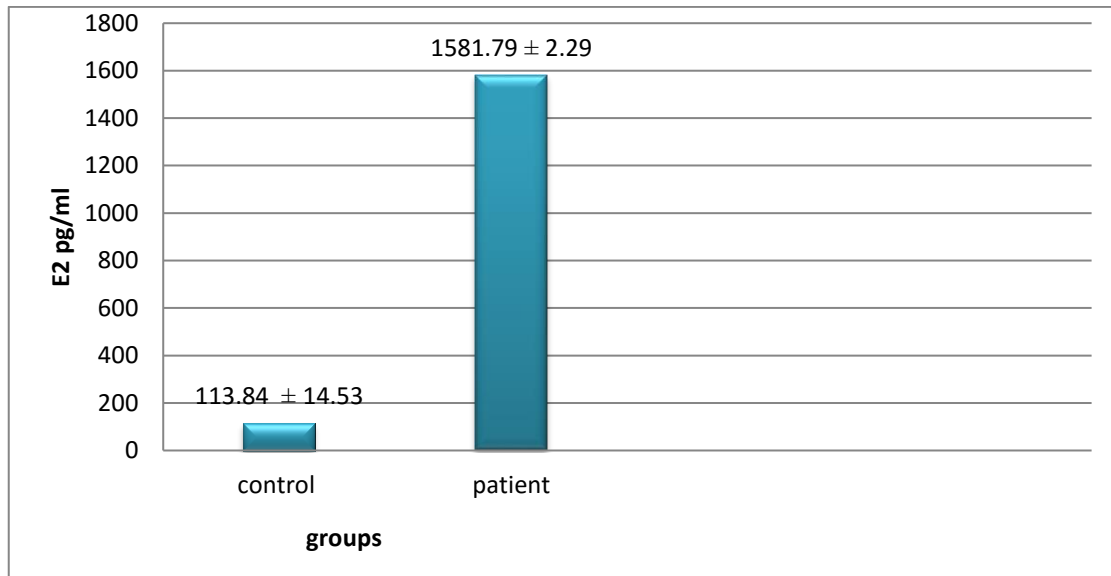


Figure 3: Serum E2 levels of control and breast cancer women groups.

Elabscience, USA. the results were expressed as mean \pm standard deviations (mean \pm SD). One way ANOVA-test was used to compare parameters in different studied groups. P-values ($P \leq 0.05$) were considered statistically significant.

RESULTS

In this work we determined the effect of these disease on the Serotonin, Melatonin, Estradiol, and Adiponectin hormones

The levels of serum Serotonin, Melatonin, and Adiponectin hormones were showing significant decrease in breast cancer patients as compared to control group whereas the levels of Estradiol showed a significant increase in breast cancer patients in comparison to control subjects.

DISCUSSION

Breast cancer is the most widely tumor among women worldwide. Approximately 246,000 new cases of invasive breast cancer are expected to be diagnosed in the United States in 2016, and almost 40,450 will die from the illness (Joney S., 2016). Regardless of the substantial improvement in breast cancer prognosis and survival, it is still the leading cause of cancer mortality in low- and middle-income countries and more than half of the breast cancer mortality is accounted from low and middle-income countries (Ahmedin J. *et al.*, 2010, Torre L. *et al.*, 2012). In general, serotonin has a participant role in several vital cell pathways when it is involved in the cell proliferation,

apoptosis and platelet aggregation (Elshayeb E. *et al.*, 2016).

Decreased of serotonin levels at cancerous patients group after treatment with chemotherapy or radiotherapy may disclose as reflex to the decrease in the abnormal (cancerous) cells utilizing toxic therapy. Thusly, the decrease in the serotonin concentration may decrease the vascularity of harmful cell then increase necrosis that finally leads to increase of cancer cell mortality.

Li W., *et al.* (2015) provided no evidence to support the hypothesis that shift work increases breast cancer risk. They suggested that the effect of shift work on breast cancer risk may be different in Asian and Caucasian women.

Bonde J., *et al.* (2012) summarized the evidence from epidemiological and experimental studies and presented possible recommendations for prevention of the effects of night work on breast cancer. Among those investigations that quantified duration of shift work, there were statistically significant elevations in risk only after about 20 years working nightshift. Authors suggested that it is unclear from these studies whether or not there is a modest but real elevated risk for shorter durations. Disruption of the diurnal melatonin secretion example can be decreased by restricting the number of consecutive night shifts. Reddish light and decreased light intensity during work at night could potentially help diminish the inhibitory activity of light with strong intensity on the melatonin secretion, but further mechanistic insight is required before definite suggestions can be made. They concluded that preventive effects of melatonin

Table 4: Serum Adiponectin concentrations of (control) and (breast cancer) groups.

Group	n	Adiponectin concentrations (ng/ mL) mean \pm SD
control	55	6.74 \pm 1.69 ^a
Breast cancer	85	0.50 \pm 0.11 ^b
LSD		0.23

- Legend as in table (1)

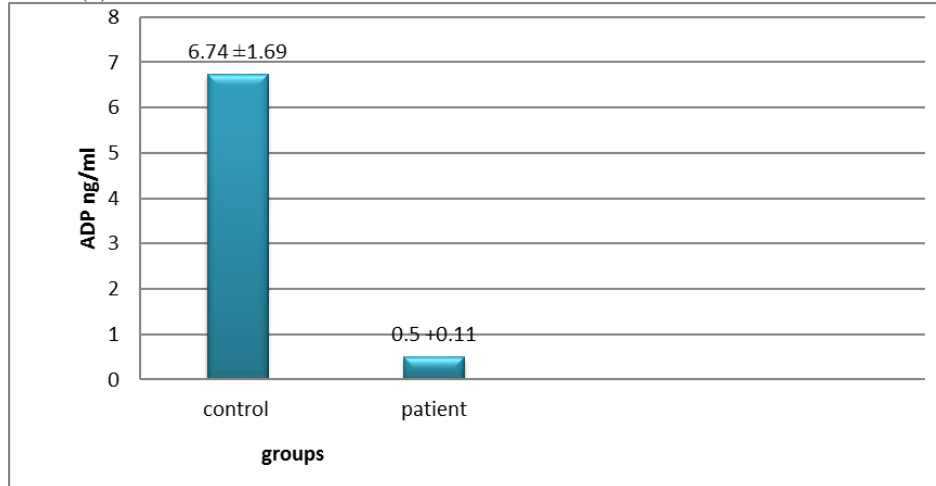


Figure 4: Serum ADP levels of control and breast cancer women groups.

supplementation on breast cancer risk have not been obviously documented, but may be a promising avenue if a lack of side effects can be shown even after long-term administration.

Subsequently, Tamarkin *et al.* found that women with ER-positive breast cancer had a reduced nocturnal increase in melatonin, and observed an inverse correlation between ER levels and peak melatonin values. (Tamarkin L. *et al.*, 1982). In relation to the role of estrogens in the genesis and development of mammary tumors, it is important to consider that two-thirds of breast cancer occurs in postmenopausal women, where ovaries have ceased to be functional and circulating levels of estrogens are low. Nevertheless, in these cases, the concentration of estradiol (E2) in breast tumors is higher than in plasma and normal breast tissue (Landeghem A., 1985).

Adiponectin has been inversely associated with estrogen levels. Remains possible that adiponectin may influence breast cancer risk by modifying flowing estrogen levels (Nalabou *et al.*, 2014).

In Several studies have demonstrated that low serum adiponectin levels are related with increased risk for breast cancer (Chlebowski R. *et al.*, 2005, Mohan R. *et al.*, 2012). After few years in Iraqi Baghdad, Tabaan *et al.* conducted a study on 48 breast cancer females and 41 apparently healthy as a control group.

They found that serum adiponectin was significantly lower in breast cancer cases compared to controls ($P < 0.001$), and an inverse association between serum level of adiponectin and breast cancer (Tabaan *et al.*, 2014).

CONCLUSION

From the data presented in this study, we could obtain the following conclusions:-

In Breast cancer patients, we finding decrease in Serotonin (ST), Melatonin (MT), and Adiponectin (ADP) Hormones. While we finding increase in Estradiol (E2) in Breast cancer patients as compared to control group.

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