



# INFLUENCE OF BREAST CANCER ON SERUM TESTOSTERONE AND SEX HORMONE BINDING GLOBULIN LEVELS AMONG SUDANESE LADIES

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## ABSTRACT

**Background:** Breast cancer is the most frequent cancer and the second leading cause of cancer deaths among women worldwide and an increasing incidence rate has been observed in Sudan.

**Objective:** this study was aimed to determine the effect of breast cancer on testosterone and sex hormone binding globulin in Sudanese female patients.

**Materials:** This study included 120 untreated breast cancer patients with clinical and histopathological evidence and 100 healthy volunteers as a control. Venous blood was drawn from the cases and controls.

**Methods:** Testosterone and sex hormone binding globulin were estimated in blood samples by using radio-immune assay. Paired t-test was used to compare the mean serum levels of testosterone and sex hormone binding globulin between patients and controls.

**Results:** In the present study there were significant high levels of serum testosterone in premenopausal lady patients with breast cancer as compared to control group (p value <0.05). On the other hand, there were significant low levels of sex hormone binding globulin in ladies with breast cancer when compared to controls (p value <0.05).

**Conclusion:** A significant high level of testosterone and low level of sex hormone binding globulin were found in this study.

**Key Words:** Testosterone, Sex hormone binding globulin, Breast cancer

## INTRODUCTION

Breast cancer is a malignant tumor starts from the breast tissues and cells. Breast cancer affects 13% of women during their lives. Cancers originating from ducts are known as ductal carcinomas; those originating from lobules are known as lobular carcinomas [1]. In 2008 breast cancer caused 458,503 deaths worldwide, it is compromises 13.7% of the total cancer deaths among women. Breast cancer is more than 100 times more common in women than breast cancer in men, although males tend to have poorer outcomes due to delays in diagnosis [2]. The primary risk factors for breast cancer are sex, age, lack of childbearing or breastfeeding, higher estrogen levels, race, socioeconomic status and dietary iodine deficiency [3].

Testosterone is a steroid hormone and is found in mammals, and other vertebrates. In human, testosterone is

originally secreted in male testes and female ovaries. It is the major male sex hormone and an stimulating steroid [4]. In men, testosterone plays a major role in the developing of the male reproductive system particularly testis and prostate as well as progressing the secondary sexual characteristics like increased muscle, bone mass and the growth of body-hair. In addition, testosterone has important role in human health and well-being addition to the prevention of osteoporosis [5]. On average, an adult human male produces about ten times more testosterone than an adult human female, but females are more sensitive to the hormone [6].

About sixty to seventy percent of secreted testosterone is bound to special type of protein so named sex hormone binding globulin (SHBG). Sex hormone binding globulin (SHBG) is a glycoprotein which possesses high affinity for 17 beta-hydroxysteroid hormones such as testoster-

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one and oestradiol. It is synthesized in the liver, plasma concentrations being regulated by, mainly androgen/oes-trogen balance along with other factors such as thyroid hormones, insulin and dietary factors. The main function of this protein is transporting of sex steroids in plasma. The concentration of sex hormone binding globulin is a major factor regulating their distribution between the protein-bound and free states. The exact role of the protein in the submission of hormones to target tissues is not yet clear. Measurement of sex hormone binding globulin is used to evaluate androgen metabolism disorders and in identification of women with hirsutism who are more likely to respond to estrogen therapy [7]. Testosterone/sex hormone binding globulin ratios correlate well with both measured and calculated values of free testosterone and help to differentiate subjects with excessive androgen activity from normal individuals [4].

Sex hormone binding globulin levels is controlled by feedback mechanism factors. The negative feedback factors include insulin, insulin-like growth factor 1, transcortin and hyperandrogenism. Whereas, the positive feedback factors of sex hormone binding globulin levels include high levels of growth hormone, estrogen and thyroxin hormone [7]. Increased sex hormone binding globulin level results in increasing of total testosterone level. Reference ranges for serum sex hormone binding globulin is ranged between 40 to 120 n.mol/L for premenopausal females, and 28 to 112 n.mol/L for postmenopausal females [8]. True androgen status can be determined by measuring the free testosterone or by calculating total testosterone / sex hormone binding globulin ratio, which known as the free androgen index (FAI) [9].

The expected testosterone levels for women are lower than the normal levels for men. The testosterone levels in women are set according to the stages of life [3]. Girls before puberty comprise the minimum levels of testosterone due to their body's stage of development. Then, during puberty, testosterone is started to be produced from adrenal glands with other sex hormones and making pre-menopausal women have the second-highest levels of testosterone [10]. As a woman begins being aged, she produces more testosterone, less estrogen and other female sex hormones. Therefore, menopausal and post-menopausal women have the highest levels of testosterone [11]. High testosterone levels in women can cause many problems including growth of facial and body hair, deep voice, and aggressiveness [12].

The aim of this study is to examine the role of alterations in testosterone and SHBG in woman developing breast cancer.

## MATERIALS AND METHODS

This was a cross sectional case-control study conducted period between 2011 and 2014 in Khartoum State, Sudan. The study included 100 normal healthy persons (control) and 120 untreated breast cancer patients with clinical and histopathological evidence, from the out patients and hospital admissions of the Radiation and Isotopes Center Khartoum (RICK). All selected participants were premenopausal women, and the ages of them were 28-50 years, and all of them with no history of smoking or biochemical evidence of diabetes, hormonal disorders, hypertension, hyperlipidaemia, renal or liver disease or family history of the breast cancer. This study was approved by the ethical committee of Omdurman Islamic University. Informed consent was obtained from each participant. Fasting 10ml venous blood was drawn between 6-10 a.m. and serum was separated and analyzed within 3 hours after collection. Then testosterone and sex hormone binding globulin tests were estimated by radioimmunoassay (RIA) an automated techniques as described by Choudhury et al [13]. Statistical analyses were performed using SPSS (Statistical Package for Social Sciences). Differences in mean values between groups were evaluated by a one-way analysis of variance (ANOVA) and Student's t-test. Statistical analysis where the value of p<0.05 was considered as significant.

## RESULTS

Table 1 showed comparison the mean serum levels of testosterone between patients and control groups. Serum testosterone level was increased significantly in breast cancer when compared with the controls.

**Table 1: Serum testosterone in patients compared to control group: Values are mean±SD**

	Controls	Breast cancer	P value
Number	100	120	0.814
Age (years)	30.5 ± 6.085	31.2 ± 8.551	1.00
Testosterone (ng/dl)	40.6 ± 10.7	61.5±5.4	0.023

Table 2 showed comparison the mean serum levels of SHBG between patients and control groups. Serum SHBG level was increased significantly in breast cancer when compared with the controls.

**Table 2: Serum sex hormone binding globulin in patients compared to control group: Values are mean±SD**

	Controls	Breast cancer	P value
Number	100	120	0.814
Age (years)	30.5 ± 6.085	31.2 ± 8.551	1.00
sex hormone binding globulin (nmol/l)	57.1±9.9	33.3±7.6	0.007

## DISCUSSION

Like other cancers, breast cancer, exists due to an interaction between a defective gene and the environment. Normal cells divide as many times as needed and stop. They attach to other cells and stay in place in tissues [14]. Sex hormones play an important role in etiopathogenesis of breast cancer. Sex hormone binding globulin modulates the functions of testosterone and estradiol by altering their bioavailability to target tissues. Recently, it has been suggested that sex hormone binding globulin also functions as a regulator of the steroid hormone signaling system in the cells, by binding to its specific membrane receptor [8].

In the present study, there were significant high levels of serum testosterone (p value<0.05) in premenopausal ladies patients (61.5±5.4 ng/dl) with breast cancer compared to controls (40.6 ± 10.7 ng/dl). Different studies have provided evidence that hormonal environment can be altered with changes in lifestyle factors. Sedentary lifestyle, characterized by reduced physical activity and a diet rich in fat, refined carbohydrates, and animal protein is associated with high prevalence of overweight, metabolic syndrome, insulin resistance, and high plasma levels of several growth factors and sex hormones, most of these factors are associated with breast cancer risk [15].

Also in this study there were significant low levels of sex hormone binding globulin (p value<0.05) in premenopausal ladies patients (33.3±7.6 nmol/l) with breast cancer compared to controls (57.1±9.9 nmol/l). Many studies showed positive associations between sex hormones and breast cancer risk. Bhaskaran et al [16] reported that the contribution of androgens to breast cancer risk is increased their role as a substrate for estrogen production. Biro et al [17] also found that low levels of sex hormone binding globulin may indicate high levels of bioavailable steroid hormones.

## CONCLUSION

Breast cancer was significantly increased the levels of testosterone and low level of sex hormone binding globulin significantly in Sudanese patients.

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