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Insulin, estradiol levels and body mass index in pre- and post-menopausal women with breast cancer

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ABSTRACT

Breast cancer is the most common cancer among women where it is associated with considerable morbidity and mortality. The aim of this study was to investigate the association between insulin, estradiol levels and body mass index (BMI) as risk factors for breast cancer. Methods: 80 women newly diagnosed with breast cancer stage I–III invasive breast cancer, were selected randomly and divided in two groups: 40 pre-menopausal aged 26–46 years and 40 post-menopausal aged 52–90 years. Radioimmunoassay used for serum insulin levels measurement, ELISA was used for estradiol levels and BMI calculated by weight (kg)/height (m^2). Results: Insulin levels in premenopausal (16.6 ± 10.5) and postmenopausal (17.9 ± 8.8); breast cancer patients showed increasing pattern from the normal levels (4.0–16.0 μIU/ml). While, the levels of estradiol in premenopausal (233 ± 173) and postmenopausal, (549 ± 468); estradiol level in postmenopausal was higher than normal level (50–300 ng/ml), its level showed significantly increase in postmenopausal breast cancer (P.Value = 0.001). Conclusion: Insulin levels increased in pre- and post-menopausal breast cancer patients while estradiol levels do not showed association with premenopausal breast cancer. High BMI, high insulin and estradiol levels in post-menopausal women may be considered as risk factors for breast cancer.

1. Introduction

Breast cancer is one of the most common types of cancer that affects millions of women around the world (Parkin, Ferlay, & Pisani, 2005). Insulin level is one of the established risk factors for breast cancer (Muti et al., 2002); it may be associated with common risk factors such as high body mass index (BMI). Insulin is an important metabolic hormone that affects body fat mass (Gisela, 2005). Estradiol is important in sexual

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development and other body functions. It is produced mainly in the ovaries in premenopausal women, and mainly in fat tissue in postmenopausal women. Estradiol in the blood is linked to an increased risk of breast cancer in women after menopause (Key et al., 2011). Hormone balance that may promote breast cancer growth include elevated levels of circulating or tissue estrogens and insulin which have been a key role in the development and progression of breast cancer (Pollak, 2008); some studies in Western countries have found associations between higher BMI and a higher risk of death among women with breast cancer (Masaaki et al., 2012), although other studies have found no such association (Barnett et al., 2008).

2.   Materials and methods

A cross sectional study of 80 Sudanese women newly diagnosed with breast cancer, they were not used any medication including hormone replacement therapy, they were randomly selected to participate in the study. Serum insulin level was measured by using radioimmunoassay (RIA) with polyclonal antibody and antigen I^{125}labeled (Beijin Isotope Nuclear Electronic Machine Co. LTD, China). The normal range of insulin level is from 4.0 to 16.0 μIU/ml while estradiol levels were measured by ELISA kits with normal range (50–300 ng/ml) and BMI was calculated using the following equation [weight (kg)/height (m^2)]. The patients were classified as underweight 18.5, normal weight in ranged 18.5–24, over weight in ranged 25–29.9 and obese ≥30 (kg/m^2).

2.1.   Statistical analysis

Data analyzed by using the computer program SPSS version 20.0 for frequencies, percentage, mean and standard deviation. Linear correlations were performed by using the Pearson's Correlation Coefficient, r. $p \leq 0.05$ was considered significant.

3.   Results

The mean levels and standard deviation of insulin in both pre- and post-menopausal breast cancer patients showed increasing pattern from the normal levels premenopausal (16.6 ± 10.5) and postmenopausal (17.9 ± 8.8), and there was no significant difference (P.Value = 0.5), which may indicate that there is a relationship between high insulin and breast cancer. While, the levels of estradiol in premenopausal (233 ± 173) and postmenopausal (549 ± 468), estradiol in postmenopausal was higher than normal levels (50–300 ng/ml), it's significantly increased in postmenopausal breast cancer (P.Value = 0.001) as shown in Fig. 1. Regarding insulin serum levels there was no significant correlation with BMI in pre- and post-menopausal breast cancer patients (r = 0.0, P = 0.9 and r = 0.1, P = 0.4 respectively), also estradiol serum levels and BMI had no significant correlation (r = 0.01, P = 0.9 and r = 0.05, P = 0.7 respectively). However, insulin level in premenopausal women increased in normal weight, over weight and obese; underweight women had normal insulin
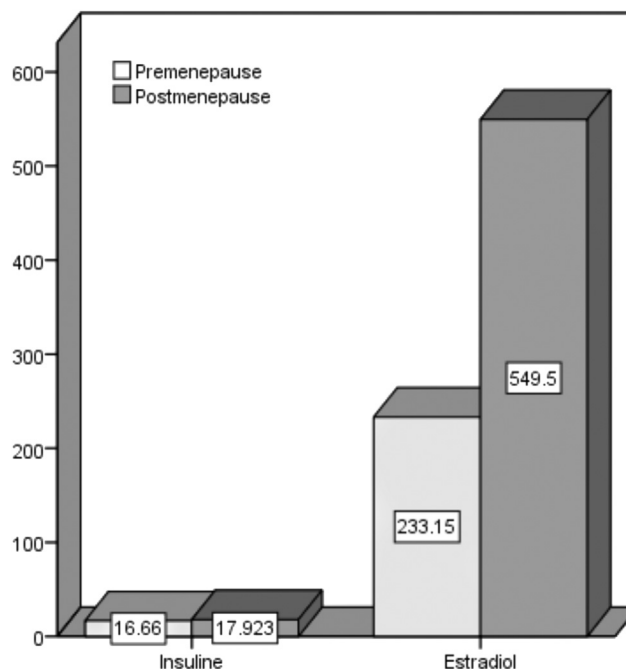

Fig. 1 – **Insulin and estradiol levels among study population.**

levels, while estradiol levels based in the normal levels as shown in Table 1. Among postmenopausal, the mean levels of insulin were increased in normal weight and obese; while estradiol levels were increased in different BMI groups as shown in Table 2.

4.   Discussion

This study demonstrated that BMI associated with insulin and estradiol levels at diagnosis. Our findings showed high insulin level in both pre- and post-menopausal women with breast cancer. In a relevant study, positive association was found between insulin level and breast cancer in both pre- and post-menopausal women (Nichols et al., 2009). Insulin has been shown to stimulate cell proliferation in normal breast tissue and in human breast cancer cells (Lawlor, Smith, & Ebrahim, 2004). In contrast another study showed that insulin level was strongly correlated with BMI in non-diabetic women newly diagnosed breast cancer (Chappell et al., 2001); the

Table 1 – The mean levels of Insulin and Estradiol among BMI groups in premenopausal women with breast cancer.

BMI (kg/m^2)	Number (%)	Mean ± SD	
		Estradiol (50–300 ng/ml)	Insulin (4–16.0 μIU/ml)
Normal weight	16 (40%)	265.1 ± 243.1	17.4 ± 12.1
Over weight	14 (35%)	195.5 ± 151.1	18.5 ± 9.3
Low weight	8 (20%)	244.9 ± 142.1	10.2 ± 1.9
Obese	2 (5%)	192 ± 45	23.1 ± 21

Table 2 — The mean levels of Insulin and Estradiol among BMI groups in postmenopausal women with breast cancer.

BMI (kg/m^2)	Number (%)	Mean ± SD	
		Estradiol (50–300 ng/ml)	Insulin (4–16.0 μIU/ml)
Normal weight	8 (45%)	495 ± 411	18.4 ± 8.0
Over weight	8 (20%)	808 ± 730	15.3 ± 8.7
Low weight	5 (12.5%)	596 ± 457	14.3 ± 5.9
Obese	9 (22.5%)	401 ± 193.9	21.3 ± 11.5

same study showed that high insulin level was seen in some non-diabetic women who had normal weight (Goodwin et al., 2002), which confirms our finding that insulin level increased in women who had normal weight in both pre- and post-menopausal women with breast cancer. Also meta-analysis study showed non-significant correlation between BMI and breast cancer risk during pre-menopausal, but a significant correlation during post-menopausal period (Pamela et al., 2002). However, among pre-menopausal women, insulin level was increased in women who had a normal weight only, finding a possible link between insulin levels and breast cancer risk is less clear in pre-menopausal women (Cheraghi, Poorolajal, Hashem, Esmailnasab, & DoostiIrani, 2012); but several studies suggested that high body mass index is associated with a reduced risk in pre-menopausal women (Eliassen, Tworoger, Mantzoros, Pollak, & Hankinson, 2007), also pre-menopausal women who are overweight or obese have a lower risk of breast cancer. Explain this relation not well understood (Norman et al., 2006); however, serum estradiol levels do not show a significant association with premenopausal breast cancer risk (Kaaks et al., 2014) which confirms our finding, while seven studies found that higher blood estrogen levels increased breast cancer risk in pre-menopausal women (Teras et al., 2011), An inverse association between BMI and risk of premenopausal breast cancer has been observed in a number of epidemiologic studies; Furthermore, premenopausal women with a high BMI have lower estradiol levels even when accounting for an ovulation (Tworoger et al., 2006). Among post-menopausal group, the insulin level was increased in normal weight and obese women, while underweight and overweight women had normal insulin level. Our findings are similar to this study showing that obesity is associated with high levels of insulin; hyperinsulinemia is an independent risk factor for breast cancer and may have a role in explaining the obesity-breast cancer relationship; Strong positive association between the risk of breast cancer and insulin levels in postmenopausal women was found (Yang et al., 2011). The poor association of obesity and breast cancer outcomes may be mediated by insulin (Gunter et al., 2009), also another study found a positive association between hyperinsulinemia and post-menopausal breast cancer only among women who had a BMI greater than 25 kg/m (Goodwin et al., 2008). Losing weight after menopause may help lower risk of breast cancer (Muti et al., 2002). Several studies considered high BMI and post-menopausal breast cancer patients is directly related to circulating estrogen levels (Lukanova et al., 2004); insulin may also play a role in breast carcinogenesis via the effects of insulin, insulin like growth factor (IGF) and the estrogen signaling pathways in breast tissue (Key et al., 2011), also hyperinsulinemia induces proliferative tissue abnormalities because of the strong anabolic effect of insulin, which results in stimulated DNA synthesis and cell proliferation (Mawson et al., 2005). The present results suggests that insulin level influence breast cancer risk through direct effects on breast cell proliferation, then metabolites affect; and post-menopausal-obesity relationship may be mediated by insulin and estrogen levels; normal weight and obesity are associated with high insulin and estradiol levels among post-menopausal breast cancer patients at diagnosis. Also normal-weight women with high insulin or estradiol levels in cancer patients were at approximately the same risk of breast cancer as obese women with high insulin or estradiol serum levels.

5. Conclusion

Insulin levels increased in pre- and post-menopausal women with breast cancer; while estradiol levels, did not show any association with premenopausal breast cancer. High BMI, high insulin and estradiol levels in post-menopausal women may be considered as risk factors for breast cancer; and weight gain must be avoided.

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