ORIGINAL ARTICLE

Type 2 Diabetes and Following Incidence of Breast Cancer in a Group of Diabetic Women

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ABSTRACT

Background: Diabetes and breast cancer are diagnosed within the same women more often than would be expecting by chance.
Aim: To evaluate the association between diabetes and incidence of breast cancer in a group of diabetic women.
Methods: Study engaged 50 diabetic women diagnosed with breast cancer. The women ranged in age from 45-55 years old. 20 age matched women with no history of any disease were taken as controls. Patients were taken from department of Oncology and local breast clinic of Lahore city. Inclusion criteria was based on the development of breast cancer after diagnosis of type 2 diabetes. Duration of study was March,2015 to Sep,2015. Insulin doses and duration of insulin treatment were recorded.
Results: Age, BMI and level of serum insulin and insulin resistance in diabetic patients with breast cancer are tabulated. It was observed that mean age of patients and normal subject was 46.0 and 45 years. Mean BMI of patients was high as compared to the BMI of controls and its showed significant difference ($P<0.05$). Level of blood sugar and serum insulin was high in patients as compared to controls and showed high significant difference ($P<0.001$). Values of insulin resistance were also high of patients as compared to the insulin resistance of controls.
Conclusion: It is concluded that middle age obese women with poorly controlled diabetes treated with high units of insulin are prone to develop breast cancer.
Keywords: Diabetes, Breast cancer, hyperinsulinemia

INTRODUCTION

Insulin is a potent growth stimulating hormone acting through insulin and insulin-like growth factor-1(IGF-1) receptors[1]. Both insulin and IGF-1 share each other's effects at high concentrations, due to weak affinity for the receptor. Insulin has miscellaneous metabolic effects. Its increased level may increases the synthesis and mitogenic activity of IGF-1 which results an abnormal proliferation of cell[2].

A direct relationship of breast cancer with diabetes is based on hyperglycemia, hyperinsulinemia and inflammation[3,4]. Hyper-insulinemia may promote breast cancer. Insulin resistance has been linked to type 2 diabetes and also increased the risk of breast cancer in diabetic women[5]. It is reported that 49% increased risk of mortality in women with diabetes in association with breast cancer. Reason may be poor prognostic characteristics including late diagnosis and suboptimal treatments in people with diabetes[6].

It is demonstrated that hyperinsulinemia stimulates proliferation of tissue abnormally, results an increase synthesis of DNA and proliferation of cell[3]. In a study it is proposed that in breast cancer cells, the receptors of insulin are over expressed and cause an activation of the phosphatidylinositol 3-kinase-Akt and mitogen-activated protein kinase pathways[8].

Hyperinsulinemia is a significant risk factor for breast cancer. Women with the high level of insulin had 1.5-fold higher risk of developing breast cancer than women with the low level of insulin. It is proposed that the endocrine/metabolic disturbances, lead to hyperinsulinemia causes the changes in the function of IGF in tissue of breast, might act in association with increased activity of estrogen[9].

Hyperinsulinemia and possibly sustained hyperglycemia are important regulators of not only the development of cancer but also of treatment outcome[10]. Higher doses of Insulin and the utilization of insulin analogue for longer period of time are related with malignant changes[11]. It is proved hyperinsulinemia play an important role in arbitrating a relationship of obesity with breast cancer[12,13].

Insulin resistance is related with an increased risk of different sites of cancer including the breast cancer[14]. Insulin resistance of the skeletal muscles, liver and fatty tissue leads to hyperinsulinemia due to raised secretory function of the beta-cells[15]. In the uncompensated stage of insulin resistance

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hyperglycemia results, this encourages tumor formation by many pathways via increased synthesis of DNA of the tumor cells[16].

Insulin resistance in skeletal muscle is manifested by decreased insulin-stimulated glucose uptake and results in impaired insulin signaling and multiple post-receptor intracellular defects including impaired glucose transport, glucose phosphorylation, reduced glucose oxidation and glycogen synthesis[17]. The relationship between tumor promotion, insulin and insulin resistance shows new options in the treatment and prevention of cancer. Role of insulin in etiology of breast cancer and prognosis has established increased attention. Study was therefore designed to evaluate the association between diabetes and occurrence of breast cancer in a group of diabetic women taking insulin for treatment.

MATERIAL AND METHODS

This study engaged 50 diabetic women diagnosed with breast cancer. Patients were taken from department of Oncology and local breast clinic of Lahore city. Duration of study was March 2015 to Sep 2015. Inclusion criteria was based on the diagnosis of breast cancer after type 2 diabetes. Insulin doses and duration of insulin treatment were recorded. About 75% of the cancers were hormone-receptor-positive. All the women were treated with chemotherapy. The women ranged in age from 45-55 years old. 20 age matched females with no history of any disease were taken as controls. The study was approved by the Bioethics Committee of Institution. The study was carried out in accordance with suitable version of Declaration of Helsinki.

Statistical Analysis: Data was entered and analyzed by SPSS 18.0. Variables were expressed as mean±SD. These were compared by student 't' test. P<0.05 was taken as significant.

Table: Age, BMI and level of serum insulin and insulin resistance in diabetic patients with breast cancer.

Variables	Patients (50)	Controls (20)
Age (years)	46.0±10.2	45.0±4.6
BMI (Kg/m^2)	28.4±5.6*	24.7±3.5
Blood sugar random (mg/dl)	200.45±25.8**	145.8±13.6
Serum Insulin (uIU/mL)	8.09±6.29**	3.2±2.5
Insulin Resistance	4.0	1.2

**P< 0.05= Significant difference*
***P<0.001 = Highly significant difference*

RESULTS

Age, BMI and level of serum insulin and insulin resistance in diabetic patients with breast cancer are tabulated. It was observed that mean age of patients and normal subject was 46.0 and 45 years. Mean BMI of patients was high as compared to the BMI of controls and its showed significant difference (P<0.05). Level of blood sugar and serum insulin was high in patients as compared to controls and showed high significant difference (P<0.001). Values of insulin resistance were also high of patients as compared to the insulin resistance of controls.

DISCUSSION

Though the relationship between neoplasm and diabetes is known, the different sites of cancers are more common in diabetic patients. The factors which increases the risk of cancer in diabetic people is not fully understood[18,19].

Mean age of diabetic patients with breast cancer and normal subject was 46 and 45 years. However a study reported that mean age of diabetic patients with breast cancer and normal subject was 52.1 and 59.1years[5]. It is reported that increased age and use of insulin is strongly linked with increase risk of cancer in diabetic people[3].

Mean BMI of diabetic patients with breast cancer and normal subject was 28.4 and 24.7 kg/m^2. A study also found an increased BMI in patients (30.7 vs 25.0) as compared to the BMI of controls[5]. According to a study BMI ≥30 kg/m^2 was linked with increased risk of cancer[3]. The results of a study observed a direct relationship between the increase mass of adipose tissue, hyperglycaemia and inflammation and suggested the role of obesity in linking cancer with diabetes[20]. However a study found that insulin resistance and fasting insulin level (metabolic health parameters) may be more biologically related with risk of breast cancer than obesity[13].

We observed significant hyperglycemia in patients as compared to controls. Data of a study reported that prolonged hyperglycemia leads to production of reactive oxygen species in cells which have mutagenic effect and cause the damage of DNA[21,22]. Additionally high level of glucose provides energy to cancer cells, and may speed up tumor growth[23].

Our study observed significant hyperinsulinemia in diabetic patients with breast cancer. Recently a study proposed that ErbB2 Receptor Tyrosine Kinase 2 is intensified in breast cancer and related with poor diagnosis. It is suggested that there is link between the signaling of ErbB2, insulin and insulin-like growth factor (IGF). ErbB receptors bind and phosphorylate insulin receptor substrates and this mediated the process of anti-estrogen resistance in cancer of breast[24]. Another study found that hyperinsulinemia is may be due to the impairment of pathway of phosphatidylinositol-3 kinase/Akt in cancer[25].

We found that hyperglycemia and hyperinsulinemia increased the insulin resistance in diabetic women with breast cancer. A study demonstrated that an increased insulin resistance is related with decreased survival of breast cancer[26]. Another study reported that metabolic derangements characteristic of diabetes (i.e. insulin resistance, hyperglycemia and hyperinsulinemia), increases the risk of some cancers. Study further demonstrated that diabetes may affect the process of neoplasm either by hyperglycemia or by insulin resistance[27].

The limitations of our study include its observational and retrospective design, and comparatively small sample size which has not permitted to reveal other possible relationships for which helpful trends are noted.

CONCLUSION

It is concluded that middle age obese women with poorly controlled diabetes treated with high units of insulin are prone to develop breast cancer. Studies are required to find out the pathophysiologic communications between diabetes and breast cancer to resolve whether proper diabetic care can decrease mortality in patients with breast cancer.

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