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Diabetic type 2 and breast cancer marker CA 15.3 value

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ABSTRACT

In this study we intended to assess the serum tumor marker CA 15.3 among diabetic females in comparison to non diabetic females without neoplasia and any other diabetic complication. Results indicate that there is statically significance between diabetic and non-diabetic females, although the levels are within the normal range of method used. It reveals that serum tumor marker CA 15.3 is useful in the monitoring purpose only.

Key words: Diabetes, Tumor marker CA 15.3, Glycemic control

INTRODUCTION

Epidemiological evidence has indicated that both pre- and postmenopausal women with insulin resistance, metabolic syndrome and type 2 diabetes (T2DM) have an increased breast cancer (BC) risk [1].Breast Cancer is the second most common cancer in the world. A report of the American Cancer Society showed about 1.3 million American women diagnosed with BC and about 0.5 million die from the malignancy [2,3]. Saudi Arabia is no exception, where, cancer of breast is most commonly prevalent. There is paucity of detailed published epidemiologic data and updated account of the figures registered. An earlier report according to Saudi National Cancer Registry reported an increasing proportion of BC among women of different ages from 10.2% (2000) to 24.3% (2005) [3], and affecting population which is younger than found in the West [4]. The unwarranted connection between diabetes mellitus (DM) and breast cancer has gained new ground in recent years. DM is diagnosed in the age group of 30+ years with possible exposure to predisposing factors like hyperisulinemia and obesity at younger age. Furthermore, 12% of the breast cancer cases are diagnosed in the young females aged 20-34 years [5]. Genetic predisposition and environmental factors such as high fat diet accompanied with sedentary life style constitute increased breast cancer risk. Thus, metabolic abnormalities including obesity and type 2 diabetes (T2DM) are positively associated with the breast cancer risk [6,7]. Diabetic condition induces changes in several hormonal systems, including insulin, insulin like growth factors, estrogens and other cytokines that may affect the breast cancer risk. Characteristics of T2DM including insulin resistance and the resultant hyperinsulinemia are strongly correlated with postmenopausal as well as pre-menopausal breast cancer risk [8,9].

High fasting glucose levels were directly correlated with breast cancer risk both in pre-menopausal and postmenopausal women [9,10]. Studies also indicate that fasting glucose levels ≥ 126 mg/dl, which is cutoff for defining the T2DM were related to an increased risk for the carcinogenesis of the breast [10,11]. In addition, reduced HDL-cholesterol and increased blood pressure have contributed to increased risk for breast cancer [12,13].

Thus, type 2 diabetic status, with its multiple risk factors, appears to be an important contributor of breast cancer risk.

For breast cancer, there is currently very few serum markers used clinically. Some studies have identified the protein CA 15.3 as possible breast cancer marker [14,15].Trape et al [16] listed the values of different Tumor markers without neoplasia in different disease. In our literature search we did not find the value of the breast cancer marker CA 15.3 among diabetic females. Hence, in this study we intended to determine the CA 15.3 in diabetic females.

MATERIALS AND METHODS

Study Design & subjects
This case - control study was conducted on a group of type 2 diabetic females (age 15 – 60 years (n=60) who attended at the diabetes clinic, King Fahd Specialist Hospital, Qassim. Diabetes was defined by fasting blood glucose ≥7.0 mmol/L (126 mg/dL), the use of hypoglycemic agents, or both. They were never diagnosed for any cancer. The control group (n=60) include healthy individuals who were recruited from public places. They were neither had been diagnosed as having diabetes nor use hypoglycemic medicationnor be hypertensive or any known medical condition.

Blood sampling
Venous blood sample collected from each subject after informed consent in one heparinized vacutainer (4 ml) and one plain vacutainer (4 ml) to obtain plasma and serum respectively. All blood tubes were maintained at 4^0C during transportation to the laboratory. After centrifugation at 3000 rpm for 15 min, aliquots of plasma and serum were stored at -80˚ C until analysis.

Estimation of plasma blood glucose and HbA1c
Plasma glucose levels were determined by end-point enzymatic method (Glucose oxidase-glucose peroxidase) using kits manufactured by Human Diagnostics, Wiesbaden, Germany.

Glycated hemoglobin (HbA1c) was measured from whole blood by Latex turbidimetric method using commercially available kit supplied by Vital Diagnostic, Italy.

Breast tumor markers:
Breast cancer markers CA 15.3 was determined using kits manufactured by Human Diagnostics, Wiesbaden, Germany

Measurement of Body mass index (BMI)
Body weight and height were recorded for each subject. Body mass index (BMI) was calculated as weight (in kilograms) divided by height (in metres) squared. The WHO classification for BMI was used to determine the degree of obesity (World Health Organ Tech Rep Ser 1995).

Statistical analysis:
The data collected and analyzed using the statistical package for social sciences (SPSS) software (version 17). Results expressed as mean ±SD or number (percentage) as appropriate. Comparison of variables between patients and controls was performed by student t-test for continuous variables. We assessed for possible correlations between CA15.3and selected variables (glucose, HbA1C, Duration of DM and age) using Pearson correlation test. The p values < 0.05 were considered significant.

RESULTS AND DISCUSSION

Characteristics of the Study Participants

Table 1. Demographic and clinical characteristics of the study subjects, comparing type 2 diabetic patients to healthy (non-diabetic) subjects

Variable	Patients n=60	Controls n=60	*p*-value
Age (yr)	56.54±9.5	45.66±11.3	.000*
Weight (kg)	75.97±13.3	72.59±15.4	.253
Height (cm)	160.9±5.5	159.7±14.6	.572
BMI (kg/m^2)	31.92±5.8	31.39±8.1	.699
Blood Glucose (mg/dl)	225.12±87.1	82.64±24.1	.000*
HbA_{1c} (%)	9.51±2.3	4.97±1.6	.000*
Duration of DM (years)	9.53±6.2	----	……

Abbreviations: BMI, body mass index; DM, diabetes mellitus; HbA1c, glycosylated haemoglobin.Data presented as mean ±SD for all variables.
** P-value <0.05; compared type 2 diabetic patients to nondiabetic healthy subjects*

Table: 2 Breast cancer marker CA 15.3 expressed in (Mean±SD) in diabetic and healthy subjects

	Diabetic	control	p-value
CA 15.3	8.88± 6. 8	6.278±3.9	0.006

P-value <0.05; compared type 2 diabetic patients to non-diabetic healthy subjects

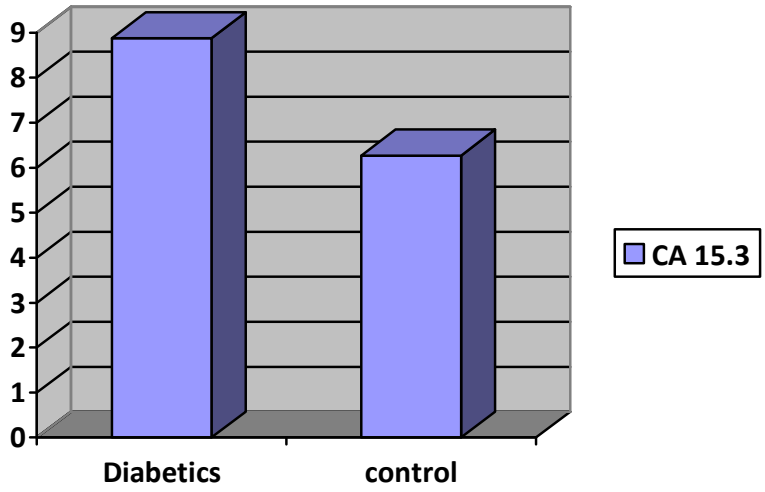

Fig 1: Mean CA15.3 levels in Type 2 diabetic and to non-diabetic healthy subjects

In recent decades, several biomarkers have been investigated as predictors of breast cancer risk, development, prognosis, and treatment efficacy. The detection of biomarkers that strongly associated with breast carcinogenesis has an enormous potential, especially for selecting subjects at high risk of developing breast cancer who could benefit from chemo preventive treatments. Although the number of potential biomarkers continues to increase, a unique biomarker for breast cancer risk prediction has not been identified [16].CA 15.3 is the most widely used serum biochemical tumor marker in breast cancer [17]. It is a carbohydrate antigen secreted from the mammary epithelial cells [18]. Assay of CA 15.3 is a relatively convenient and noninvasive method for evaluating prognosis in newly diagnosed breast cancer patients [19]. In our study we found that the CA 15.3 levels in both groups withinthe normal levels mentioned in the kit insert (< 37 U/L). However, there was a statistical significant difference between the patients and controls. Data from meta-analysis indicated that women with type 2 diabetes have a 23% higher risk of developing breast cancer compared with non-diabetic [20]. Pearson correlation test shows CA 15.3 value among diabetic is independent of age (P value=0.863), duration of DM (P value =0.172), HbA1C (P value =0.954), Glucose (P value =0.193). Diabetes can be considered as a risk factor for breast cancer independent of obesity and age. But the biological mechanisms are still unclear [21].CA 15-3 is an antigen localized at the luminal aspect of breast epithelium. Since the early 1990s, antibodies against CA 15-3 have been developed as possible serum markers of

occult and recurrent breast carcinoma. Moreover CA 15-3 is more specific for breast cancer and is also more sensitive in patients with advanced disease. [22].

CONCLUSION

Estimation of CA 15.3 level for the screening to assess the risk of breast canceramong diabetics is merely useful.

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Recommendation
Since the number of participants, both Diabetics and controls, enrolled in the present study was limited; further studies on larger sample size are required to determine the consistency of these observations among various levels of glycemic control and various complications of diabetes

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