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Serum level of prostate-specific antigen (PSA) in women with breast cancer

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ABSTRACT

Objective: To identify the diagnostic role of total and free prostate-specific antigen (TPSA and FPSA) in breast cancer in women.
Methods: Blood samples of 55 women with breast cancer were prospectively analyzed for PSA before and after breast surgery, with a control group of 82 healthy women.
Results: Total and free PSA levels were significantly higher in women with breast cancer (preoperatively) than in healthy women ($P < 0.001$). Both serum TPSA and FPSA showed a significant decline in their pre-surgical values after surgical removal of the tumor ($P < 0.001$). A significant proportion of breast cancer patients (83.6%) had free PSA as the predominant molecular form in serum as compared to 0% of controls and 1.8% of postoperative groups ($P < 0.001$). TPSA and FPSA levels were significantly associated with younger age and earlier cancer stage, whereas no significant association was found between these two variables and FPSA as a predominant molecular form.
Conclusions: This study indicated a clinical significance of preoperative measurement of serum TPSA and FPSA in the diagnosis of women with breast cancer, and may be a useful marker for monitoring the response to treatment.

1. Introduction

Worldwide, breast cancer is by far the most common cancer among women, with an incidence rate more than twice that of colorectal cancer and cervical cancer and about three times that of lung cancer [1].

In Iraq during the 5-year period 2000–2004, 63,923 Iraqi patients with various types of newly diagnosed cancer were registered by the Iraqi Ministry of Health from all Iraqi provinces with the exception of three Northern provinces (Sulaimanyia, Erbil, and Dohouk); of these patients, 31,652 (49.5%) were females, and breast cancer alone accounted for 31% of all new cancer cases among females [2]. In Basrah, breast cancer constituted one-third of all cancers in women in 2005, with an incidence rate of 13.1/100,000 women. The annual mortality rate of breast cancer in Basrah in 2005 was 3.2/10,0000 [3].

Although prostate-specific antigen (PSA) is the most valuable tumor marker for the diagnosis and management of prostate carcinoma [4], it is widely accepted that PSA is not prostate-specific [5]. Numerous studies have shown that PSA is present in some female hormonally regulated tissues, principally the breast and its secretions. The serum PSA concentration in females is approximately 1000-fold less than that in males (0.004 mg/L) [6].

PSA is produced by the majority of breast tumors and may be a favorable indicator of prognosis in breast cancer [7,8]. However, other studies have reported a lack of value of PSA as a prognostic marker in breast cancer patients [9,10].

Low levels of PSA are released into the female circulation, and while the level of serum PSA is elevated in both benign and malignant breast disease, the molecular form of circulating PSA differs between women with and without breast cancer [11]. The two major molecular forms of PSA (i.e. free and complexed forms) are differently accumulated in the serum of healthy women and women with diseased breasts. In the vast majority of sera of healthy women and patients affected by benign breast diseases, PSA seems mostly to be bound to α1-antichymotrypsin (ACT), whereas in a significant proportion of females with breast cancer the predominant serological form is the free form of PSA (FPSA). The ratio of FPSA to total PSA (TPSA) may have value as a simple biochemical test for the diagnosis of breast pathologies, including breast cancer [7,8]. These findings indicate that PSA may have a potential diagnostic utility in breast cancer [11].

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The aim of this study was to measure and compare the relative values of free PSA and PSA complexed with the serine protease inhibitor ACT in the serum of women with breast cancer and women with no known malignancies to identify the diagnostic role of PSA in breast cancer, and to analyze its association with the severity of the disease process.

2. Subjects and methods

This case–control study was conducted in Basrah from October 2008 to December 2009. The study was approved by the ethics committee of College of Medicine, Basrah University, and informed consent was obtained from all participants.

2.1. Subjects

Cases included 55 women with newly histologically confirmed breast cancer without any other malignancy who were admitted to the surgical wards of Basrah General Hospital and Al-Sadr Teaching Hospital during the period of the study. None of them had had preoperative chemotherapy or radiotherapy before sampling. Those patients were followed up for 1 month postoperatively before they received any chemotherapy or radiotherapy. In addition, 82 apparently healthy women free from cancer on a clinical basis and free from disabilities who attended the outpatient department of the aforementioned hospitals were chosen by a simple random sampling as a control group.

2.2. Data collection

Both groups (cases and controls) were interviewed according to a special questionnaire designed for the purpose of the study, covering aspects related to socio-demographic characteristics and medical history (past and present).

2.3. Biochemical analysis

After an overnight fast, blood samples (5 mL) were collected by venipuncture using a sterile disposable syringe in a plain plastic tube. The blood samples were centrifuged at 3000 rpm for 10 min; the sera were stored frozen (−20 °C) until analysis. In cases, blood samples were obtained preoperatively (prior to any surgical or other therapeutic procedures) and postoperatively (after a follow-up of 1 month post-mastectomy). Serum FPSA and TPSA were measured using a sandwich-type enzyme-linked immunosorbent assay (ELISA) technique using immunoassay kits with an analytical sensitivity of 0.05 ng/mL [12].

2.4. Statistical analysis

Statistical analyses were done using SPSS (Version 17). The results are presented in tables. Data were expressed as means and medians. Differences were assessed using chi-square, *t*-test or ANOVA where applicable.

Table 1
Characteristics of breast cancer (BC) cases and control groups in this study.

	BC patients	Controls	*P*-value
Number	55	82	
Mean age (range)	49.1 (32–72)	48.1 (32–71)	0.682
Married, number (%)	52 (94.4)	72 (87.8)	0.153
Postmenopausal, number (%)	18 (32.7)	24 (29.3)	0.667
BC stage, number (%)			
I	0		
II	17 (30.9)		
III	27 (49.1)		
IV	11 (20.0)		

PSA concentrations in serum were categorized into three groups based on the minimum detection limit of the assay procedure (0.05 ng/mL) as follows: PSA < 0.05 ng/mL; PSA between 0.050 and 0.67 ng/mL; and PSA > 0.67 ng/mL. Using the contingency table and chi-square test (or Fisher's exact test when necessary), we compared the differences in proportions of PSA concentrations between breast cancer patients and normal women, between pre-surgical and post-surgical serum, and among pre-surgical patients according to age, premenopausal status and stage of the disease. The *P*-value of <0.05 was considered significant.

3. Results

The mean age of cases was 49.1 ± 11.1 years, whereas the mean age of controls was 48.1 ± 10.7 years.

As shown in Table 1, no significant differences were noted between cases and controls regarding age, marital status, and postmenopausal state. About half the breast cancer patients had stage III cancer.

As shown in Tables 2 and 3, serological TPSA and FPSA were significantly associated with younger age (≤50 years) and premenopausal status. There was a negative association between total and free PSA with increasing age ($P < 0.001$). The PSA levels were significantly higher in premenopausal breast cancer patients than in postmenopausal counterparts ($P < 0.001$).

As shown in Table 4, the serum levels of TPSA, and FPSA, as well as the FPSA/TPSA ratio, were higher among patients with breast cancer (preoperatively) as compared with controls with a highly significant difference ($P < 0.001$).

Both serum TPSA and FPSA in addition to the FPSA/TPSA ratio showed a significant decline in their pre-surgical values after surgical removal of the tumor (Table 5).

As shown in Table 6, the TPSA was significantly higher among postoperative cases as compared with controls, whereas no significant difference was noted in the serum level of FPSA and FPSA/TPSA ratio of postoperatives and controls.

The proportions of patients with a higher serum level of TPSA (≥0.68 ng/mL) were significantly higher among (preoperative) patients with breast cancer as compared with controls. Similarly, the proportion of patients with a higher serum level of TPSA

Table 2
Comparison of serum total prostate-specific antigen (PSA) between preoperative breast cancer cases and controls according to age and menopausal status.

Character	Cases (preoperative)	95% CI		Controls	95% CI		*P*-value
		Lower	Upper		Lower	Upper	
Age							
≤50 years	1.609 ± 0.922	1.302 ± 0.667	1.887 ± 1.131	0.645 ± 0.386	0.538 ± 0.329	0.792 ± 0.439	<0.001
>50 years	0.959 ± 0.524	0.761 ± 0.375	1.190 ± 0.624	0.307 ± 0.264	0.219 ± 0.204	0.417 ± 0.310	
Menopausal status							
Premenopause	1.605 ± 0.883	1.306 ± 0.651	1.919 ± 1.078	0.625 ± 0.375	0.519 ± 0.320	0.704 ± 0.419	<0.001
Postmenopause	0.895 ± 0.558	0.611 ± 0.415	1.133 ± 0.638	0.256 ± 0.246	0.174 ± 0.165	0.367 ± 0.327	