Original Article

Detection of Serum Prostate Specific Antigen in Lactating, Pregnant, and Advanced Breast Cancer Sudanese Women.

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ABSTRACT

Introduction: Although prostate-specific antigen (PSA) is the most valuable tumor marker for the diagnosis and management of prostate carcinoma, it is widely accepted that PSA is not prostate specific.

Objectives: The aim of this study is to address the possibility of using the PSA as marker for the sex assignment in different categories and relevance of this test in women problems.

Method: We have evaluated the measurement of serum total PSA for differentiation between Sudanese women with advanced breast cancer (n= 10), and those are lactating (n=10), pregnant (n=10) compared with 20 healthy women as control group.

Serum total PSA (TPSA) was measured using immuno-radiometric assay (IRMA).

Results: In this study the mean age was significantly higher advanced breast cancer groups compared with lactating group (P<0.01). The mean serum PSA levels in the healthy control women examined (n=20) was 0.72 ± 0.55 vs. 1.18 ± 0.92, 1.42 ± 2.43 and 0.51 ± 0.13 ng/ml in serum from advanced breast cancer (n=10), pregnant (n=10) and lactating women (n=10) respectively. A significant high level of total PSA in serum of advanced breast cancer compared with the normal group (P< 0.05).

Conclusion: These results indicated the possible use of total PSA to distinguish between healthy women and/or women with advanced breast cancer.

Key words: Prostate-specific antigen, Total PSA, Breast cancer, Sudanese women

Prostate-specific antigen (PSA) has been biochemically and molecularly characterized as a 33-kDa androgen dependent glycoprotein related to the kallikrein family of serine proteases, with chymotrypsin and kallikrein-like enzymatic activity[1, 2].

Prostate specific antigen (PSA) is well-established tumor marker for the diagnosis and management of prostate cancer. With the advent of more sensitive methodologies for PSA detection and measurement came the finding that PSA is not prostate specific, but is present in female tissues, predominantly the breast and its secretions[3].

Since the initial discovery of PSA in females, numerous normal and pathological tissues and bodily fluids have been reported to have PSA immunoreactivity. PSA is detectable in healthy breast tissue[4, 5], and is present in breast tumors[6, 7] and breast cystic disease[4, 8, 9]. Various breast secretions contain PSA, including nipple aspirate fluid (NAF)[10, 11], the milk of lactating women[12], and breast cystic fluid[8, 13]. Endometrial tissue produces PSA[14], as do ovarian tumors[15], and PSA is present in amniotic fluid and maternal serum during pregnancy[12, 16- 18]. Low levels of circulating PSA are detectable in female sera[19].

We have previously evaluated the usage of F/T PSA and PAP (prostate acid phosphatase) as tumor markers in Sudanese patients[20]. However, measurement of PSA in pregnant

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and advanced breast cancer women as well as in normal females was not done.

The aim of this study is to address the possibility of using the PSA as marker for the sex assignment in different categories and relevance of this test in women problems.

MATERIALS AND METHODS

In this prospective study, we examined 10 patients with advanced breast cancer at the Institute of Nuclear Medicine, Molecular Biology, and Oncology (INMO). Those patients were histologically and ultrasonography confirmed with breast cancer (BC) without any other malignancy. Advanced breast cancer patients with a history of active heart disease, organ failure, diabetes, acute infections in the previous 4 weeks were excluded from this study. Blood was also drawn from pregnant women (n=10), and lactating women (n=10) referred to the department of Obstetrics and Gynecology at Medani Maternity Hospital. Samples were obtained from the excess blood taken for their relevant conditions.

The control group included 20 healthy women between the age 10 and 75 years who revealed no breast cancer pathology and not pregnant or lactating as well. The age, age at menarche, parity and body max index were recorded for each participant.

All the study subjects gave informed consent to the study, which was approved by the Institutional Medical Ethics Review Board of the University of Gezira.

Blood samples were collected in 5 ml sterile vacutainers containing ethylene diamine tetra acetic acid (EDTA). After blood clotting, the samples were centrifuged within 20 minutes after collection at 500 x g for 10 min, and sera were stored at -20 ºC until assay.

The free and total prostate-specific antigens were assessed using an immunoradiometric assay (Skybio, London, UK) based on two anti-PSA antibodies: ^{125}I- labeled and other one as solid phase. All tubes were counted for 100 seconds on multi-well gamma counter. The standard curve was drawn as (% bound/total counts) vs. log free PSA concentration. Quality control and samples were determined by interpolation. The mean, standard deviation and percentiles were calculated and the differences between means were analyzed using student unpaired t-test. All data were analyzed by using the SPSS computer program and the $P<0.05$ was considered to be statistically significant.

Results

Ten patients with advanced breast cancer were enrolled in this prospective study. Table 1 presents the distribution of the mean ages± SD of different groups.

There was high significant difference ($P<0.01$) in the age between lactating and advanced breast cancer groups.

The lowest mean concentration of total PSA in serum samples was reported in the lactating group, and the highest one was in the pregnant group despite the insignificant difference between them.

Discussion:

Earlier reports has suggested that immunoreactive prostate specific antigen (IR-PSA) positivity of breast tumors is a favorable prognostic indicator for women with breast cancer[21, 22] and that high serum levels of PSA in women might represent a valuable diagnostic marker in breast cancer[23, 24]. In this study we are trying to investigate for the presence of PSA as a marker in Sudanese women with different categories (lactating, pregnant and advanced breast cancer) and to see whether this marker could be favourable prognostic indicator. Our previous study indicated the usefulness of measuring PSA in the differential diagnosis of prostate carcinoma (PCa) and benign prostatic hyperplasia (BPH) in Sudanese patients with prostate enlargement[25].

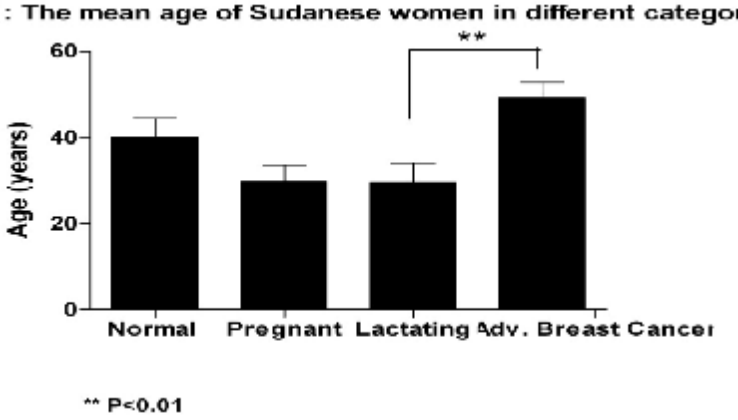
We measured the total PSA in serum- not in milk- of lactating women in order to compare it with that in serum of other study subjects, because there was reported considerable variation in the concentration of PSA which was mostly present as free PSA[25]. Furthermore the major difficulties encounter the detection of free PSA in serum led us preferentially to use total PSA instead of free PSA.

Table 1: distribution of the patients according to age of the lactating, pregnant, advanced breast cancer and healthy women as control group.

Clinical data	*Lactating group (Mean ± SD)*	*Pregnant group (Mean ± SD)*	*Adv. Breast cancer group (Mean ± SD)*	*Control (Mean ± SD)*	***P*-value**
Age (years)	29.6 ± 14.5**	29.8 ± 12.0	49.3 ± 11.0**	40.2 ± 18.8	P<0.01

** P<0.01

Figure1: The mean age of Sudanese women in different categories



** P<0.01

Table 2:

Means, medians and ranges of total prostate specific antigen in the serum of lactating, pregnant and advanced breast cancer women compared with healthy women as control group.

Groups		Total PSA (ng/ml)		
		(Mean ± SD)	Median	Range
Lactating	(n=10)	0.51 ± 0.13	0.50	0.3 – 0.8
Pregnant	(n=10)	1.42 ± 2.43	0.50	0.1 – 8.2
Adv. Breast cancer	(n=10)	1.18 ± 0.92*	1.30	0.1 – 2.6
Control	(n=20)	0.72 ± 0.55*	0.60	0.1 - 1.9

In this study we found a significant deference in the age between advanced breast cancer and lactating females and that was accompanied with an increase or decrease in the total PSA. This notion supported the data that total PSA concentration decreases with women's age[23]. This also indicated the possible association between the high levels of total PSA and the progression of breast malignancy. Supportive evidence reported the remarkable presence of PSA in female's breast tumors that are positive to steroid hormones receptor. It was also found to be associated in patients with early stage disease and age less than 50 years[26, 27]. Romppanen et al.[28] reported an association between the age and the decrease of total PSA in normal control and breast cancer patients which was in agreement with our results.

We found high significant level of total PSA in women with advanced breast cancer compared with the normal subjects. This result was in agreement with others who reported high levels of serum total PSA in both benign and malignant breast cancer[23, 29]. Recent study has proposed PSA as a new marker for the assessment of benign breast tumors[29].

It is important to note that the number in this study is too small to reach firm conclusions. Nevertheless, our finding of serum total PSA in breast tumor, lactating and pregnant women together with the data presented by others[28, 30] suggest that PSA can no longer be regarded as specific prostatic marker. However, it can be used to distinguish between healthy women and/or women with advanced breast cancer.

Further studies with large sample size are required to prove our finding.

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