

EVALUATION OF TOTAL PROSTATE-SPECIFIC ANTIGEN IN MALIGNANT AND BENIGN BREAST LESIONS IN WOMENDuaa Knaj^{1*}, Michael Georgeos¹, and Faisal Redwan²¹Department of Oncology, Tishreen University Hospital, Latakia, Syria.²Department of Laboratory Medicine, Tishreen University Hospital, Latakia, Syria.

*Corresponding Author: Duaa Knaj

Department of Oncology, Tishreen University Hospital, Latakia, Syria.

Article Received on 27/08/2024

Article Revised on 16/09/2024

Article Accepted on 06/10/2024

ABSTRACT

Background: Prostatic specific antigen is a significant biomarker for the diagnosis and monitoring of prostate cancer. Initially regarded as a prostate-specific marker, subsequent evidence has demonstrated its presence in females as well. Material and methods: The study was conducted with two groups of women. Group A included 50 patients with breast cancer, who were divided into 3 categories. (A1=10) Patients with histologically confirmed malignancy were admitted to the oncology center after biopsy and prior to surgery. (A2=30) patients were admitted following to surgical resection of the tumors. (A3=10) patients with metastatic tumors. Group B (30) patients with benign breast lesions. Serum PSA levels were analyzed for each patient in both groups, with a second measurement taken after six-months for patients in category A1. A comparison of PSA levels was conducted between the different categories of group A, as well as between group A and B. The impact of the histological pattern of benign lesions on PSA levels was investigated. Results: The mean total PSA values for both groups were as follows: A1 (1.4), A1-1 (0.51), A2 (0.52), A3 (1.61) and B (0.26) ng/ml. PSA levels were greater in cases of metastatic breast cancer compared to non-metastatic disease ($p < 0.05$). The mean PSA was elevated in all breast cancer cases when compared to benign lesions, with a statistically significant difference ($P < 0.05$). Our findings revealed that PSA levels were elevated in fibrocystic lesions when compared to the other patterns observed in Group B. Conclusion: Total PSA may prove a benefit in differentiating between benign and malignant breast lesions in women.

KEYWORDS: prostatic specific antigen, PSA, total, breast cancer, benign.**INTRODUCTION**

Prostate-specific antigen (PSA) is an important biomarker in the diagnosis and monitoring of prostate cancer. It has a molecular weight of 33 kilo Dalton (kDa) and is secreted by the columnar epithelium of the prostate.^[1] PSA was thought to be secreted only by the prostate gland and then found only in males; however, subsequent studies have proved that it is present in females and in many other tissues and biological fluids, including skene glands, breast, ovaries, uterus and salivary gland.^[2] PSA has been observed in many cancerous conditions including those affecting the breast, colon, ovary, uterus, and kidney. It has also been found in physiological conditions in women, such as pregnancy and lactation, as well as in healthy women.^[3] Given the critical importance of early diagnosis in breast cancer to enhance treatment efficacy and prognosis, it is essential to have diagnostic methods that are both feasible and demonstrate high sensitivity and specificity. Nevertheless, the development of blood-based diagnostic tests that can identify cancer at an early stage and predict treatment response has proven challenging. The objective of this study was to quantify serum PSA levels in women

with benign and malignant breast lesions, and to assess the role of PSA in these settings.

MATERIALS AND METHODS

This case-control study, conducted at the oncology center of Tishreen University Hospital in 2023, included 80 patients, who were distributed into two groups: Group A comprised 50 patients with histologically confirmed malignancy in the breast. The patients were divided into three categories: Category A1 (n=10) for patients with tumors diagnosed by biopsy and before any treatment; TPSA was measured in serum samples from the same patients six months after surgery (A1-1). Category A2 (n=30) included patients admitted to the Oncology center after surgical resection of breast tumors. Category A3 (n=10) included cases of metastatic breast cancer. Group B consisted of women with benign lesions of the breast. Patients were recruited in accordance with the established inclusion and exclusion criteria. Informed consent was obtained from all participants. The study population consisted of patients aged 18 years-old and above, not currently pregnant or in the postpartum period, and without a history of other malignancies.

Patients who did not meet the aforementioned criteria were excluded from the study. A total PSA analysis was conducted on patients in both groups at the time of their admission to the oncology center.

Blood samples of 5ml were obtained from each patient in both groups. Subsequently, the samples were left at room temperature for a period of 10 to 15 minutes to allow for clotting. Following this, the samples were placed in the centrifuge for a further 5 minutes. Subsequently, the serum was separated from other components. The samples were stored at a temperature of -20°C until further analysis could be conducted.

Statistical analysis

All data were subjected to analysis using the statistical software package SPSS. All results were expressed as mean values \pm standard deviations. Subsequently, the results were subjected to further analysis to ascertain any significant differences between the mean values \pm SD. This was achieved through the use of either a t-test or an analysis of variance (ANOVA), as appropriate. A p-value of less than 0.05 was considered to indicate statistical significance. Serum total PSA was analyzed using an enzyme-linked immunosorbent assay (ELISA) method, with a detection limit of 0.005 ng/ml.

RESULTS

The study consists of two distinct groups: Group A comprises patients aged between 28 and 64 years, while

Group B consists of patients aged between 20 and 58 years. Patients with breast cancer were (29 patients below the age of 50 and 21 patients above the age of 50). The mean serum TPSA levels for both groups were as follows: A1 (1.4 ng/mL), A1-1 (0.51 ng/mL), A2 (0.52 ng/mL), A3 (1.61 ng/mL) and B (0.26 ng/mL) (Table 1). A comparison of data within Group A revealed that the mean PSA level in A1 was higher than that observed in A2 ($P = 0.000$). A comparison of TPSA levels between A1 and A3 revealed that the mean PSA level in A3 was higher than that in A1. Furthermore, the mean PSA level for A3 was also higher than that for A2. In all three cases, the P-value was less than 0.05, indicating that the observed differences in levels were statistically significant. The mean PSA values recorded six months following surgery (A1-1) were found to be lower than that observed prior to the surgery (A1). The comparison between Group A and Group B revealed that the mean levels of TPSA in categories A1, A2, and A3 were higher than those observed in the benign Group B.

The distribution of benign breast lesions according to histological type is presented in Table 2. It includes 15 fibro adenomas, 12 fibrocystic lesions, and 3 inflammatory lesions. The mean PSA levels for these lesions were 0.23, 0.31, and 0.17 ng/ml, respectively.

Table 1: The different mean total PSA values of group A, B.

	Range	Minimum	Maximum	Mean	Std. Deviation
A1	.48	1.13	1.61	1.40	.14866
A1-1	.09	.46	.55	.510	.03251
A2	.65	.33	.98	.520	.15985
A3	.34	1.48	1.82	1.61	.10573
B	.24	.15	.39	.2600	.05356

The mean total PSA value for Group A was found to be statistically different from that of Group B.

The highest level of prostate-specific antigen (PSA) in group B was observed in fibrocystic lesions, followed by fibroadenomas. In contrast, the lowest PSA level was observed in case of inflammatory lesions. The p-value

for this analysis was 0.000, indicating that the observed difference in mean PSA levels was statistically significant ($p < 0.05$).

Table 2: The difference in TPSA level according to benign breast lesions.

		N	Mean	Std. Deviation
Total PSA	Fibro adenomas	15	.2380	.02366
	Fibrocystic	12	.3100	.03464
	Inflammatory	3	.1700	.01732
	Total	30	.2600	.05356

DISCUSSION

Prostate-specific antigen (PSA) is a serum tumor marker that has been successfully employed for the diagnosis and management of prostatic cancer.^[4] The main function of PSA in males is to liquefy the seminal clot, thereby facilitating fertilization, which represents its principal role.^[5] Nevertheless, significant evidence indicates that this protein is not exclusively confined to

the prostate; rather, it has been detected in various tissues and body fluids beyond the prostate.^[6]

A significant research has been conducted to investigate PSA level in women with benign and malignant breast lesions. The finding of our study showed that total PSA level was higher in women with malignant breast lesions compared with women who had benign breast lesions.

This finding is in contrast to the findings of Black *et al.*^[7] They evaluated total and free PSA levels in women with breast cancer, breast cysts and also healthy controls. They reported that patients with breast cysts had significantly higher levels of total PSA than pre-surgical breast cancer patients. A further study by Prakruti Dash *et al.*^[8] comprising three groups of women revealed no statistically significant difference in free and total PSA values between patients with benign and malignant breast lesions. However, these values were higher than those observed in healthy women.

In a study conducted by Lancelot Lobo *et al.*^[9], three groups were included (breast cancer, benign lesions and healthy women). The study found that total PSA levels were higher in the breast cancer group compared to the benign breast lesions as well as in healthy women. These results may be useful in differentiating between benign and malignant breast lesions, which is consistent with the results of our study. Razavi *et al.*^[10] also showed that TPSA levels were higher in breast cancer rather than benign lesions. The P value was statistically significant. Elevated PSA in breast cancer compared to benign breast lesions may be due to a hormonal imbalance, leading to the appearance of the hormone-dependent PSA gene.^[11]

The present study demonstrates a reduction in PSA levels six months post-surgery, a finding that aligns with the results of numerous other studies.^[7, 10] In a study including three groups of patients with breast cancer, benign lesions, and a control group of healthy women, Elteza Tahjiba Jahir *et al.*^[12] demonstrated that both total and free PSA values decreased following surgical intervention. This indicates that PSA is secreted from the tumor tissue itself, resulting in a decrease in serum values following tumor removal.

We found in our study that PSA levels were greatest in metastatic breast cancer, which may be explained by the metastatic tumor cells producing PSA or the increased tumor mass stimulating PSA production.^[11] A study done by Lancelot Lobo *et al.* revealed that PSA levels were elevated in both the fibrocystic and fibro adenoma patterns compared to other healthy breast lesions.^[9]

CONCLUSION

The main findings of our study suggest a potential correlation between total PSA and breast cancer. Serum levels were observed to be elevated in cancer cases in comparison to benign lesions, and this may prove the importance of PSA as useful tool in differentiate between benign and malignant breast lesions. Further research is required to elucidate the role of PSA as a potential biomarker in the diagnosis and follow-up of women breast cancer, as recent studies have been showed.

ACKNOWLEDGEMENT

The authors would like to express their gratitude to the Departments of Oncology, Laboratory Medicine, and

General Surgery at Tishreen University Hospital for their valuable contribution to the completion of this study.

Funding

Self-funding

REFERENCES

1. G.M. Yousef, E.P. Diamandis, The new human tissue kallikrein gene family: structure, function, and association to disease, *Endocr. Rev.*, 2001; 22(2): 184–204.
2. Yu H and Berkel H. Prostate-specific antigen (PSA) in women. *J La State Med Soc*, 1999; 151(4): 209-13.
3. Melegos DN, Yu H, Allen LC, Diamandis EP: Prostatespecific antigen in amniotic fluid of normal and abnormal pregnancies. *Clin Chem*, 1996; 29: 555–562.
4. Mashkoo FC, Al Asadi, Al Naama LM, Serum levels of prostate specific antigen (PSA) in women with breast carcinoma. *Cancer epidemiol*, 2013; 6: 145-146.
5. M Robert, B F Gibbs, E Jacobson, C Gagnon. Characterization of prostate-specific antigen proteolytic activity on its major physiological substrate, the sperm motility inhibitor precursor/semenogelin I, *Biochemistry*, 1997; 36(13): 3811–3819.
6. E.P. Diamandis, H. Yu, New biological functions of prostate-specific antigen? *J Clin. Endocrinol. Metab*, 1995; 80(5): 1515–1517.
7. Margot H. Black. Serum Total and Free Prostate-specific Antigen for Breast Cancer Diagnosis in Women. *Clinical Cancer Research*, February 2000; 6: 467–473,.
8. Dash P, Pati S, Mangaraj M, Sahu PK, Mohapatra PC. Study of serum total PSA and free PSA in breast tumours. *Ind J Clin Biochem*, 2011; 26(2): 182-86.
9. Lancelot Lobo, Rochelle Felicidade Antao, Nawin Kumar, Abhijit Sudhakar Shetty, Praveen Mahantesh Pawar, Shruti Mujumdar. Evaluation of Serum Prostate Specific Antigen as a Biomarker for Breast Carcinoma. *Surg. Gastroenterol. Oncol.* 2021 eCollection July 02 DOI: 10.21614/sgo-eC-254.
10. Seyed Hasan Emami Razavi, Mahsa Ghajarzadeh, Alireza Abdollahi, Ludmila Taran, Saeed Shoar, Ramesh Omranipour. Is Serum Prostate-specific Antigen a Diagnostic Marker for Benign and Malignant Breast Tumors in Women? *MAEDICA – a Journal of Clinical Medicine*, 2015; 10(2): 107-111.
11. Li Zhang, Xiuwei Yu, Lin Zhou, Yuan Yang, Shengchun Liu. Diagnostic value of total prostate specific antigen (TPSA) in women with breast cancer in the molecular subtyping era. *JBUON*, 2018; 23(5): 1316-1324.
12. Elteza Tahjiba Jahir, Runi Devi, Bibhuti Bhushan Borthakur.
13. Study of Serum Total PSA and Free PSA as an Oncological Marker in Breast Tumour. *Journal of Clinical and Diagnostic Research*, 2017 Mar; 11(3): BC13-BC16.