ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 05 | May - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

SERUM PROSTATE SPECIFIC ANTIGEN AS A DIAGNOSTIC AND PROGNOSTIC MARKER IN BREAST CANCER

General Surgery

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ABSTRACT

Objectives: To compare the Total serum Prostate Specific Antigen (PSA) between women with benign breast disease and malignant breast diseases **Material & Methods:** Present comparative study was conducted among the patients with benign and malignant breast cancer undergoing treatment in general surgery department of Aarupadai Veedu Medical College. The patients were analysed for the total and free PSA as important marker in differentiating the malignant from benign condition and also changes post-surgical period. The data were entered in excel sheet and analysed using SPSS v21 operating on windows10**. Result:** In present study, total of 100 patients fulfilling inclusion criteria are included with mean age of 48.53yrs. The malignant lesions showed with presence of micro calcification on mammography in (20%), (24%) with bone metastasis, (18%) with liver metastasis, (36%) with vascular invasion and (34%) with Perineural invasion. Malignant lesion were significantly higher among the women in menopausal period (78%) compared to the benign lesion (42%) ($p<0.05$).On assessment of pre-surgery, the total PSA and free PSA was more than 4ng/ml more common in malignant cases compared to the benign cases. Similarly, post- surgery, the total and free PSA were lower than 2.5ng/ml in both the groups comparable with no significant difference. On comparison of the blood parameters, there is significant higher level of blood glucose, cholesterol, LDL cholesterol, Urea and creatinine among the malignant cases compare to the benign ($p<0.05$) **Conclusion:** The present study found higher level of total and free PSA among the patients with malignant breast disease in comparison to the benign breast disease. Also post-surgery, there is significant drop in the level of both total and free PSA among the patients.

KEYWORDS

Prostate specific Antigen, Benign breast disease, Malignant breast disease

INTRODUCTION:

Breast cancer being the single biggest cause of cancer related deaths in a developing nation like India, the need for early diagnosis and appropriate treatment at the earliest is of top priority. Due to growing awareness about the breast cancers more and more number of women are being diagnosed at a relatively early stage when compared to the past. But still breast cancer related mortality remains a major concern.[1,2]Though radiological and clinical examination are available as screening programmes, the need for a serum marker which can detect disease, and the change in concentrations of which, can predict prognosis and outcome arises. Though tumor markers are of limited use in detecting breast cancers, extensive research is being done to explore new and more sensitive and specific markers. Serum PSA which initially was thought to be produced only by the prostate was surprisingly found in breast tissues and hence the question of it being used as a marker for breast diseases, mostly in breast cancers was highlighted but none of the studies done till date reach a clear consensus as to whether serum PSA is of definite value in diagnosing and predicting prognosis of breast cancers or not.[3,4]A non-invasive diagnostic procedure for the detection of malignant breast cancers will be an useful tool for screening as well as detecting new cases. Comparison of Total Serum Prostate Specific Antigen in Benign Breast Disease vs. Malignant Breast Diseases.[5,6] The Prostate Specific Antigen is Tumour marker used to detect other malignancies. Its role in diagnosing Breast Cancer is an under studied topic and hence more research on this will add valuable information to the field.Hence the present study designed to compare the Total serum Prostate Specific Antigen (PSA) between women with Benign breast disease vs. Women with Malignant breast diseases.

MATERIAL&METHODS:

This diagnostic comparative study was conducted among women of 20 to 70 years presenting with breast lump to department of General surgery of Aarupadai veedu medical college Puducherry from December 2020 to November 2022 for 2years with no past or present history of any other gyenocological or malignancies, Renal, Hepatic or thyroid malignancies and willing to participate were included in the study. The study population divided into 2 groups, group 1 being the women with breast lump with benign disease and group 2 being the women with cytologically proven malignancy. Data was collected regarding age, sex, socio economic staus, family history and thorough clinical and the tissue samples obtained from the breast were subjected to histopathological examination

Statistical Analysis:

All the data were collected in proforma and entered in excel sheet. The collected demographic data was summarized as frequency, percentage, mean and standard deviation. The summarised data were represented using tables, figures, bar diagram and pie charts. The mean difference between the continuous data was analysed using t-test, for follow-up data paired t-test and for categorical data Chi-square test was used to determine the significance between the parameters observed in this study. A P <0.05 was accepted as significant. Statistical analysis was performed using SPSS version 22.0 (IBM SPSS, US) software operating on windows 10

RESULTS:

The mean age of study population as 48.53yrs with Malignant lesion significantly higher among the women in menopausal period (78%) compare to the benign lesion (42%).($p<0.05$), the lower education was significantly higher in malignant cases compared to the benign. On assessment of socio-economic status, there is higher incidence of benign among higher socioeconomic people. There was no significant difference in group with respect to presence of family history, however it was present in higher incidence in malignant cases.($p>0.05$). On comparison 0f the blood parameters, there is significant higher level of blood glucose, cholesterol, LDL cholesterol, Urea and creatinine among the malignant cases compare to the benign.($p<0.05$).**(Table 1)**

Table -1

CHARACTER	Benign N(%)	Malignant(N%)	Malignant(N%)
AGE - Mean 48.53			

Menopausal - premenopausal Post menopausal	29(58%) 21(42%)	11(22%) 39(78%)	P value 13.51(0.001)*
Education-Not educated Till 5th standard More than 10th standard	5(10%) 17(34%) 10(20%)	15(30%) 23(46%) 4(8%)	 P value 12.316(0.01)*
Socio economic -status Higher Middle Lower	 4(8%) 14(28%) 32(64%)	 0(0%) 24(48%) 26(52%)	P value 7.252(0.01)*
Family history -absent -present	44(88%) 6(12%)	37(74%) 13(26%)	P value 7.252(0.01)*
Glucose - <250mg/dl >400mg/dl	27(54%) 3(6%)	1(2%) 30(60%)	P value 46.259(0.01)*
Cholesterol - <200mg/dl >239mg/dl 200-239mg/dl	24(48%) 7(14%) 19(38%)	6(12%) 16(32%) 28(56%)	P value – 16.04(0.01)*
LDL- <130mg/dl 130-159mg/dl >159mg/dl	 37(74%) 0(0%) 13(26%)	 16(12%) 20(40%) 24(48%)	P value- 45.61(0.01)*
Urea – >20 <20	 14(28%) 36(72%)	 26(52%) 24(48%)	P value 8.97(0.01)
Creatinine – 0.5 -1.4 >2	 14(52%) 36(72%)	 26(52%) 24(48%)	P value 6.00(0.01)

Mammography showed micro calcification present in 20%,USG abdomen showed liver metastasis present in 18% and chest X-ray showed bone metastasis present in 24%.Among malignant groups 36% showed vascular invasion& p53 marker found positive while 34% showed perineural invasion.On assessment of Breast cancer 36% were stage 2, 30% were stage1&3 and 4% were stage 4.On histology grading 48% were with grade 2,28% with grade 1&24% with grade 3.In patients with Benign lesion, 60% found to have fibroadenoma,rest showed fibrocystic disease&intraductal papilloma each 16% respectively.

On assessment of pre-surgery, the total PSA and free PSA was more than 4ng/ml, more common in malignant cases compared to the benign cases.Similarly post -surgery, the total and free PSA were lower than 2.5ng/ml in both the groups comparable with no significant difference shown in **(Table 2)**

Variable	Benign			Malignant		
	2.5-4 ng/ml	<2.5 ng/ml	>4 ng/ml	2.5-4 ng/ml	<2.5 ng/ml	>4 ng/ml
Pre T.PSA	28	15	4	19	17	14
Post T.PSA	15	33	2	16	33	1
Pre F.PSA	30	16	4	31	14	5
Post F.PSA	15	34	1	16	34	0

DISCUSSION:

PSA biomolecular expression in healthy and sick female breast secretions, cells, and tissues Although multiple research have strongly suggested that molecular versions of PSA may constitute a possible tool for assessing breast cancer risk, newer publications have shown contradictory results. Although multiple studies have identified novel biological function(s) for PSA in breast physiopathology, further research is needed to firmly establish PSA as a new weapon in the anticancer arsenal in breast cancer.[19]Tumor markers are of limited use in detecting breast cancers, extensive research is being done to explore new and more sensitive and specific markers. Serum PSA which initially was thought to be produced only by the prostate was surprisingly found in breast tissues and hence the question of it being used as a marker for breast diseases, mostly in breast cancers was highlighted but none of the studies done till date reach a clear consensus as to whether serum PSA is of definite value in diagnosing and predicting prognosis of breast cancers or not.[3], LDL cholesterol, Urea and creatinine among the malignant cases compare to the benign.($p<0.05$).Several authors, however, claim that PSA is a protein that is expressed by a variety 0f non-prostatic organs in both men and women. Some scientists also claim that the expression of this protein in women is strongly linked to breast and colon cancer, suggesting that it might be used as a biomarker for early detection, diagnosis, and prognosis 0f these malignancies in women.[4] Higher sPSA levels in postmenopausal breast cancer patients were linked to clinic-pathological variables such as the expression of AR protein in primary lesions. sPSA was favourably, if marginally, linked with clinic-pathological characteristics such as serum testosterone levels and AR positivity in a correlation study 0f quantitative data confined to postmenopausal metastatic breast cancer (MBC). [3]TPSA and FPSA levels were substantially linked with younger age and earlier cancer stage, but not with FPSA as the main molecular form. The study found that preoperative measurement of serum TPSA and FPSA has a clinical value in the identification 0f women with breast cancer and may be a valuable marker for monitoring treatment response.[43]PSA may be employed as a serum biomarker for breast cancer diagnosis, which will be specific, exact, cost effective, and applicable in both rural and urban Indian settings. Because 0f the test's simplicity, it may be performed in any small setting, making it accessible to people 0f various socioeconomic backgrounds. Investigating Free PSA alone or in conjunction with a simple biochemical marker might be one 0f the next diagnostic methods.[45]

CONCLUSION:

The present study found higher level of total and free PSA among the patients with malignant breast disease in comparison to the benign breast disease. Also post-surgery, there is significant drop in the level of both total and free PSA among the patients.Serum total and free PSA can become an important biomarker for detection and also prognosis of breast cancer.

REFERENCES:

1. Musrap N, Diamandis EP. Prostate-specific antigen as a marker of Hyperandrogenism in women and its implications for Antidoping. Clin Chem. 2016;62(8):1066–74. https://doi.org/10.1373/clinchem.2016.256198. Hanamura et al. BMC Cancer (2019) 19:1021 Page 10 of 11
2. Cserni G, Chmielik E, Cserni B, Tot T. The new TNM-based staging of breast cancer. Virchows Arch. 2018;472(5):697–703. https://doi.org/10.1007/s00428- 018-2301-9.
3. Perez-Ibave DC, Burciaga-Flores CH, Elizondo-Riojas MA. Prostate-specific antigen (PSA) as a possible biomarker in non-prostatic cancer: a review. Cancer Epidemiol. 2018;54:48–55. https://doi.org/10.1016/j.canep.2018.03.009.
4. Fujita K, Nonomura N. Role of androgen receptor in prostate Cancer: a review. The world journal of men's health. 2018. https://doi.org/10.5534/ wjmh.180040.
5. Mina A, Yoder R, Sharma P. Targeting the androgen receptor in triplenegative breast cancer: current perspectives. OncoTargets and therapy. 2017;10:4675–85. https://doi.org/10.2147/ott.s126051.
6. Basile D, Cinausero M, Iacono D, Pelizzari G, Bonotto M, Vitale MG, Gerratana L, Puglisi F. Androgen receptor in estrogen receptor positive breast cancer: beyond expression. Cancer Treat Rev. 2017;61:15–22. https://doi.org/10. 1016/j.ctrv. 2017. 09.006.
7. Hanamura T, Hayashi SI. Overcoming aromatase inhibitor resistance in breast cancer: possible mechanisms and clinical applications. Breast cancer. Japan: Tokyo; 2017. https://doi.org/10.1007/s12282-017-0772-1
8. Barton VN, Christenson JL, Gordon MA, Greene LI, Rogers TJ, Butterfield K, Babbs B, Spoelstra NS, D'Amato NC, Elias A, Richer JK. Androgen receptor supports an Anchorage-independent, Cancer stem cell-like population in triple-negative breast Cancer. Cancer Res. 2017;77(13):3455–66. https://doi. org/10.1158/0008-5472.can-16-3240.
9. Flores-Morales A, Iglesias-Gato D. Quantitative mass spectrometry-based proteomic profiling for precision medicine in prostate Cancer. Front Oncol. 2017;7:267. https://doi.org/10.3389/fonc.2017.00267.
10. D'Amato NC, Gordon MA, Babbs B, Spoelstra NS, Carson Butterfield KT, Torkko KC, Phan VT, Barton VN, Rogers TJ, Sartorius CA, Elias A, Gertz J, Jacobsen BM, Richer JK. Cooperative dynamics of AR and ER activity in breast Cancer. Molecular cancer research : MCR. 2016;14(11):1054–67. https://doi.org/10.1158/1541-7786.mcr-16-0167.
11. Kono M, Fujii T, Lim B, Karuturi MS, Tripathy D, Ueno NT. Androgen receptor function and androgen receptor-targeted therapies in breast Cancer: a review. JAMA oncology. 2017;3(9):1266–73. https://doi.org/10.1001/ jamaoncol.2016.4975.
12. Barton VN, D'Amato NC, Gordon MA, Lind HT, Spoelstra NS, Babbs BL, Heinz RE, Elias A, Jedlicka P, Jacobsen BM, Richer JK. Multiple molecular subtypes of triple-negative breast cancer critically rely on androgen receptor and respond to enzalutamide in vivo. Mol Cancer Ther. 2015;14(3):769–78. https://doi.org/10.1158/1535-7163.mct-14-0926.
13. Libson S, Lippman M. A review of clinical aspects of breast cancer. International review of psychiatry (Abingdon, England). 2014;26(1):4–15. https://doi.org/10.3109/09540 261.2013.852971.
14. Hayashi S, Kimura M. Mechanisms of hormonal therapy resistance in breast cancer. Int J Clin Oncol. 2015;20(2):262–7. https://doi.org/10.1007/s10147- 015-0788-5.
15. Fujii R, Hanamura T, Suzuki T, Gohno T, Shibahara Y, Niwa T, Yamaguchi Y, Ohnuki K, Kakugawa Y, Hirakawa H, Ishida T, Sasano H, Ohuchi N, Hayashi S. Increased androgen receptor activity and cell proliferation in aromatase inhibitor-resistant breast carcinoma. The journal of steroid biochemistry and molecular biology 144 Pt B:513-522. 2014. https://doi.org/10.1016/j.jsbmb. 2014.08.019.
16. Cochrane DR, Bernales S, Jacobsen BM, Cittelly DM, Howe EN, D'Amato NC, Spoelstra NS, Edgerton SM, Jean A, Guerrero J, Gomez F, Medicherla S, Alfaro IE, McCullagh E, Jedlicka P, Torkko KC, Thor AD, Elias AD, Protter AA, Richer JK. Role of the androgen receptor in breast cancer and preclinical analysis of enzalutamide. Breast cancer research : BCR. 2014;16(1):R7. https:// doi.org/10.1186/bcr3599. McNamara KM, Yoda T, Miki Y, Chanplakorn N, Wongwaisayawan S, Incharoen P, Kongdan Y, Wang L, Takagi K, Mayu T, Nakamura Y, Suzuki T, Nemoto N, Miyashita M, Tamaki K, Ishida T, Ohuchi N, Sasano H. Androgenic pathway in triple negative invasive ductal tumors: its correlation with tumor cell proliferation. Cancer Sci. 2013;104(5):639–46. https://doi.org/10.1111/cas.12121.
17. Mrklic I, Pogorelic Z, Capkun V, Tomic S. Expression of androgen receptors in triple negative breast carcinomas. Acta Histochem. 2013;115(4):344–8. https://doi.org/10.1016/j.acthis.2012.09.006
18. Hickey TE, Robinson JL, Carroll JS, Tilley WD. Minireview: the androgen receptor in breast tissues: growth inhibitor, tumor suppressor, oncogene? Molecular endocrinology

(Baltimore, Md). 2012;26(8):1252–67. https://doi. org/10.1210/me.2012-1107.
19. Lehmann BD, Bauer JA, Chen X, Sanders ME, Chakravarthy AB, Shyr Y, Pietenpol JA. Identification of human triple-negative breast cancer subtypes and preclinical models for selection of targeted therapies. J Clin Invest. 2011;121(7):2750–67. https://doi. org/10.1172/jci45014.
20. Ni M, Chen Y, Lim E, Wimberly H, Bailey ST, Imai Y, Rimm DL, Liu XS, Brown M. Targeting androgen receptor in estrogen receptor-negative breast cancer. Cancer Cell. 2011;20(1):119–31. https://doi.org/10.1016/j.ccr.2011.05.026.
21. De Amicis F, Thirugnansampanthan J, Cui Y, Selever J, Beyer A, Parra I, Weigel NL, Herynk MH, Tsimelzon A, Lewis MT, Chamness GC, Hilsenbeck SG, Ando S, Fuqua SA. Androgen receptor overexpression induces tamoxifen resistance in human breast cancer cells. Breast Cancer Res Treat. 2010;121(1):1–11. https://doi. org/10. 1007/s10549-009-0436-8.
22. Haffty BG, Yang Q, Reiss M, Kearney T, Higgins SA, Weidhaas J, Harris L, Hait W, Toppmeyer D. Locoregional relapse and distant metastasis in conservatively managed triple negative early-stage breast cancer. J Clin Oncol. 2006;24(36):5652–7. https://doi.org/10.1200/jco.2006.06.5664.
23. Tan DS, Marchio C, Jones RL, Savage K, Smith IE, Dowsett M, Reis-Filho JS (2008) Triple negative breast cancer: molecular profiling and prognostic impact in adjuvant anthracycline-treated patients. Breast Cancer Res Treat 111 (1):27–44. doi:https://doi. org/10.1007/s10549-007-9756-8.
24. Rao AR, Motiwala HG, Karim OM. The discovery of prostate-specific antigen. BJU Int. 2008;101(1):5–10. https://doi.org/10.1111/j.1464-410X.2007.07138.x.
25. Black MH, Giai M, Ponzone R, Sismondi P, Yu H, Diamandis EP. Serum total and free prostate-specific antigen for breast cancer diagnosis in women. Clin Cancer Res. 2000;6(2):467–73.
26. Hautmann S, Huland E, Grupp C, Haese A, Huland H. Super-sensitive prostate-specific antigen (PSA) in serum of women with benign breast disease or breast cancer. Anticancer Res. 2000;20(3b):2151–4.
27. Hammond ME, Hayes DF, Dowsett M, Allred DC, Hagerty KL, Badve S, Fitzgibbons PL, Francis G, Goldstein NS, Hayes M, Hicks DG, Lester S, Love R, Mangu PB, McShane L, Miller K, Osborne CK, Paik S, Perlmutter J, Rhodes A, Sasano H, Schwartz JN, Sweep FC, Taube S, Torlakovic EE, Valenstein P, Viale G, Visscher D, Wheeler T, Williams RB, Wittliff JL, Wolff AC. American Society of Clinical Oncology/College of American Pathologists guideline recommendations for immunohistochemical testing of estrogen and progesterone receptors in breast cancer (unabridged version). Arch Pathol Lab Med. 2010;134(7):e48–72. https:// doi.org/10.1043/1543-2165-134.7.e48.