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Biochemistry

SERUM FREE AND TOTAL PROSTATE SPECIFIC ANTIGEN WITH CARCINO EMBRYONIC ANTIGEN- LEVEL IN BREAST CARCINOMA AND BENIGN BREAST DISEASE :A COMPARATIVE ANALYSIS

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ABSTRACT

Introduction: Breast cancer is the commonest cancer among women in urban India. The identification of blood biomarkers for early detection of breast cancer is an important target of research. USG & Mammography, the current routine method for early detection, has a limited sensitivity for the detection of tumors in remote area & in patients with dense breast tissue .Moreover,they are available in only tertiary care hospital in India, so it is not accessible for all patients. North East India is mostly hilly region ,so women with breast disease can not reach those hospitals easily, but blood samples can be collected easily through local Health Care Delivery System .A panel of potential cancer biomarkers for breast cancer was selected in order to study their combined predictive value for early detection of breast cancer. Serum markers such as CEA, free and Total PSA were selected for the present study.

Objective: In the present Study ,an attempt was made to compare efficacy of free & total P.S.A as a tumour marker in breast carcinoma in comparison with C.E.A .

Materials & methods: Institution based case control Study conducted in North Bengal Medical College & Hospital.

Study Population :- Female patients aged 20-70 yrs has been divided into groups 1. Diagnosed breast carcinoma (by biopsy/FNAC), 2. Patients with benign breast diseases (biopsy/FNAC) and 3.Healthy control ,attending North Bengal Medical College & hospital.

Sample Size:-90 individuals (30 in each group). ELISA performed for all three tumour markers by using standard kit.

Result: Serum CEA & tPSA markers are significant in differentiating between benign and carcinoma group. **Serum CEA** is the only significant marker in differentiating between **healthy subjects and Carcinoma** group**.**

Conclusion: Serum tPSA & fPSA values are markers of diseased breast according to the present study. Serum CEA is the only relevant marker in differentiating normal and breast carcinoma group

KEYWORDS : Case Control Study,breast Cancers, Benign Breast Disease, Tumour Marker, CEA(Carcino Embryonic Antigen) ,TPSA (Total Prostate Specific Antigen),fPSA(Free Prostate Specific Antigen).

Breast cancer is the commonest cancer among women in urban India[1-7]. The identification of blood biomarkers for early detection of breast cancer is an important target of research[7-9]. USG and Mammography[9], the current routine method for early detection, has a limited sensitivity for the detection of tumors in dense breast tissue . USG& Mammography is available in only tertiary care hospital in India, so it is not accessible for all patients. Moreover North East India is mostly hilly region ,so women with breast disease can not reach those hospitals easily. This is especially common in socio-economically backward population.

Tumour markers are secreted by a wide variety of neoplastic cells. The markers could be endogenous products of metabolically highly active malignant cells or the products of newly switched on genes, which remained unexpressed in early life, or newly acquired antigens at cellular and sub-cellular levels. The appearance of a new tumor marker and increase in the concentration of a pre-existing one is related to the genesis and growth of malignant tumors and can be exploited for diagnostic purpose .Blood samples can be collected and transported easily through local Health Care Delivery system. A panel of potential cancer biomarkers for breast cancer has been emerging in recent years which has combined predictive diagnostic value for early stage of the disease[7]. Serum markers such as CEA, free and Total PSA were selected for the present study.Serum CEA has been shown to be related with breast cancer in previous studies but by itself is not discriminative enough . Several other cancer antigens have also emerged as known biomarkers for multiple cancer types, and are recently shown to be differentially expressed in breast cancer patientas well as healthysubjects .Numerous studies have demonstrated the production of PSA in breast cancer tissue[7-9].

The association of PSA with the disease process of breast tumour may be explained by its versatile biological role such as: (i) PSA acts as mitogen to breast tissue through of TGF-b (transforming growth factor b), a known mitogen of breast tissue (ii) PSA degrades fibronectin and laminin, the cellular matrix proteins, thereby facilitating local invasion (iii) It increases IGF-1, a proven mitogen of breast tissue (iv) It degrades IGFBP-3, which normally induces apoptosis in breast tissue and its degradation by PSA stimulates tumour progression . Low levels of PSA are present in female sera. Few studies have demonstrated PSA as an important biomarker that increased the inquisitiveness of the present investigator because it will in the long run be cheap and an easy- to- do parameter[6-9]. The objective of this study was to measure and compare the relative proportions of free PSA and PSA complexed to the serine protease inhibitor alpha1-antichymotrypsin in the serum of women with breast cancer or benign breast disease or women with no known malignancies.[10,]

OBJECTIVE - In the present Study ,an attempt was made to compare efficacy of free & total PSA as a predictive tumour marker in breast carcinoma in comparison with CEA .

MATERIALS & METHODS

Study area:-North Bengal Medical College & Hospital

Study Population:-Female patients aged 20-70 yrs groups has been divided into Group 1. Diagnosed breast carcinoma (biopsy/FNAC), 2. patients with benign breast diseases (biopsy/FNAC) and 3. Healthy control (diagnosed clinicallyby exclusion)attending North Bengal Medical College & hospital.

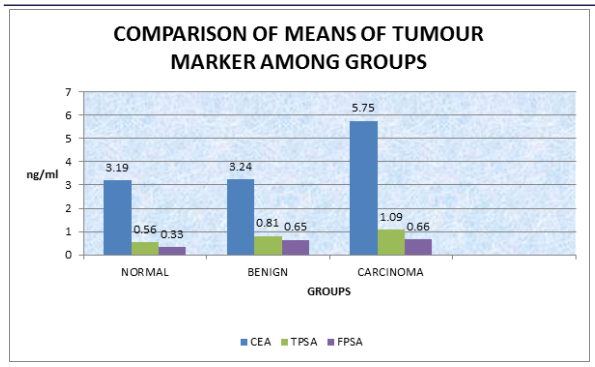
Sample Size& study design:- 90 individuals (30 in each group. Institution based Case control Study.Distribution of ages among the present study group –Normal 22.7 years(±1.68),BBD-21.4 years(±5.05),Carcinoma-43.2 years(±10).

3.Demography Pattern of this study group is mixture of rural & urban population as well as local tribal &Rajbanshis also mixed population of adjoining Bihar,Assam& local Bengalees

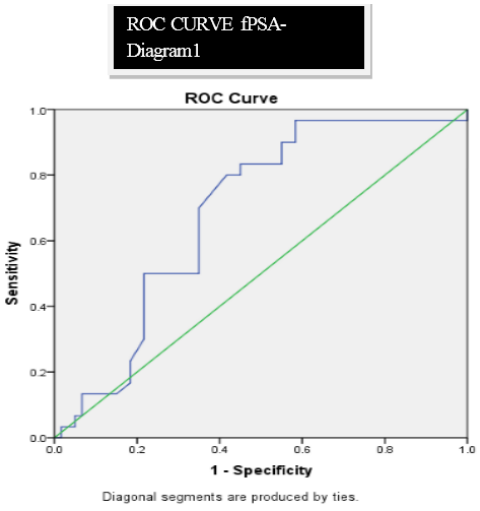
5-6 ml of blood sample collected from each patient. ELISA performed for all thetumour markers by using standard kit.

RESULTS & ANALYSIS: BY SPSS VERSION 20
MEAN±SD values of tumour markers.TABLE -A

TUMOUR MARKER	NORMAL	BENIGN BREAST DISEASE	BREAST CARCINOMA
CEA(ng/ml)	3.I9±2.26	3.24±2.12	5.75±2.56
TPSA(ng/ml)	0.56±0.31	0.81±0.29	1.09±0.32
fPSA(ng/ml)	0.33±0.21	0.65±0.34	0.66±0.28



ROC Curve of **fPSA** shows that cut off values of fPSA among normal& diseased group **is 0.58ng/ml.** Area under the curve(AUC) is **0.695.**AUC >0.5 is significant.



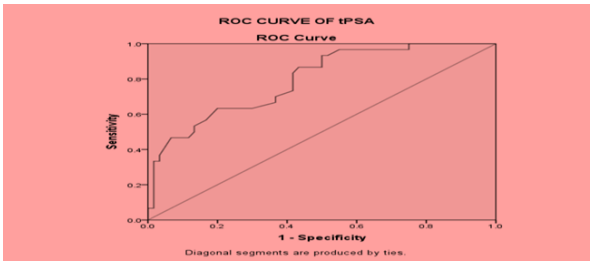


Diagram-2 ROC Curve tPSA

ROC Curve of tPSA shows that cut off value of tPSA is 0.9 ng/ml among normal and diseased group.Area under the curve is **0.79**.AUC>0.7 is highly significant.

All the Tumor Markers(TM) values are compared by Mann whitney U Test among the study groups by SPSS version 20.

Non Parametric Mann Whitney U test shows significant difference of **tPSA** values in between **benign and carcinoma group (p<0.01**). In case of **Serum fPSA** mean of ranks values in between above groups do not show any significant difference **(p=0.8)**. For **Serum CEA** difference in mean of rank values shows highly significant **values (p<0.01)** among the above groups(Table-1).

So from the above results it can be assumed that **Serum CEA & tPSA** markers are significant in differentiating benign and carcinoma groups.

DISCUSSION-The present study was conducted in a mixed population. Both rural & urban population are included in this study ,also tribal, local Rajbanshis tea garden workers and local mixed population of surrounding Bihar ,Assam, Nepal are part of this unique study population. From the present study it can be concluded that significant alteration of Serum tPSA & fPSA values occur in both carcinoma and benign breast disease group in comparison to normal healthy individuals, so they can be regarded as markers of diseased breast only ,however **Serum CEA** is the only significant marker in between **Normal and Carcinoma** group.**(p<0.01)**,also between benign carcinoma group from tables below.

	CATEGORY	N	Mean Rank	Sum of Ranks	Asymp. Sig. (2-tailed)
CEA	NORMAL	30	20.10	603.00	p<0.01
	CARCINOMA	30	40.90	1227.00	
	Total	60			

	CATEGORY	N	Mean Rank	Sum of Ranks	Asymp. Sig. (2-tailed)
CEA	CARCINOMA	30	39.93	1198.00	P<0.01
	BENIGN	30	21.07	632.00	
	Total	60			

Serum fPSA and tPSA are significant **(p<0.01)** markers in differentiating **normal and benign** breast disease groups also. **Correlation** study shows very significant correlation among fPSA & tPSA among normal & diseased group by Pearson's Correlation ratio in between normal and breast disease group.But they are not helpful in differentiating between BBD & Cancer breast.

		tPSA	fPSA	Filter Disease group
	Pearson Correlation	1	.540	0.273**
tPSA	Sig. (2-tailed)		<0.01	0.009
	N	90	90	90
	Pearson Correlation	.540**	1	0.415**
fPSA	Sig. (2-tailed)	<0.01		<0.01
	N	90	90	90

Though a tertiary care hospital and situated in urban set up, NBMC caters a group of mixed population which may not be found in many of our Medical Colleges. Tea garden labourers are unique population in our study. Breast self examination (BSE) is a remote concept for them due to lack of awareness .FNAC& Core biopsy both being invasive has their own demerits and , both of them require skilled technician and sterile O.T Set up .Here comes the utility of measuring tumor marker. 5-6 ml blood can be collected by health workers or at PHC level,for which stringent fasting condition is not required, which can be transported in bulk with other serum samples for testing to our tertiary care/SD hospitals.

So from the present study we can conclude that significant alteration of Serum tPSA&fPSA values occur in both carcinoma and benign breast disease group in comparison to normal healthy individuals ,so they can be regarded as markers of diseased breast only ,however Serum CEA is the only relevant marker in differentiating normal and breast carcinoma group.

However large retrospective study involving larger sample population &other molecular cancer markers ,histological grading and alteration of level of markers after surgery/chemotherapy could only depict the whole picture. But such a large scale study is beyond the scope of the present study because of infrastructural & funding constraint.

Elevation of Serum tPSA&fPSA values occur in both carcinoma and benign breast disease group in comparison to normal healthy individuals ,so they can be regarded as predictors of diseased breast only ,however Serum CEA is the only relevant marker in differentiating normal and breast carcinoma group .These biochemical tests can precede USG &Mamography especially in remote areas.

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