FREQUENCY OF INCREASE IN SERUM TUMOR MARKER CARCINOEMBRYONIC ANTIGEN (CEA) LEVELS IN PRIMARY BREAST CANCER (PBC) PATIENTS AT THE TIME OF DIAGNOSIS

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ABSTRACT

Objective: To determine the frequency of increase in serum tumor marker CEA levels in PBC patients at the time of diagnosis.

Study Design: Cross sectional study.

Place and Duration of Study: Oncology Department of Combined Military Hospital (CMH) Rawalpindi, from January 2014 to November 2014.

Material and Methods: Sixty three female patients with histopathologically confirmed carcinoma of breast and age range from 20 to 70 years from Oncology outpatient department (OPD) / indoor patient department at CMH Rawalpindi, were selected. All patients were staged by clinical and radiological work-up that included physical examination, all base line investigations, serum biomarkers, chest radiograph, ultrasound abdomen and pelvis, bone scan, computed tomography (CT) scan / magnetic resonance imaging (MRI) of the chest (optional). Patients serum carcino-embryonic antigen (CEA) levels were carried out only by blood sampling using chemiluminescent immunoassay with immulite 2000 CEA. Data analysis were done with the help of the Statistical Package for the Social Sciences (SPSS) version 19 software. Cut-off values of serum CEA levels >2.5 ng / ml were taken as elevated.

Results: Sixty three female breast cancer patients with histopathologically confirmed carcinoma of breast revealed elevated serum CEA levels in three stages of the disease. The median age was 47 years (range, 20-70 years). Fifteen (23.8%) patients had family history of the breast cancer. Invasive ductal carcinoma (IDCA) was the commonest histology with 60 (95.23%) patients. Most of the patients had advanced stage of the disease. Node positive cases were 53 (84.1%). The frequency of abnormal CEA levels were varying from stage II to stage IV. Elevated serum CEA levels were noted in 4 (28.6%) of stage II, 19 (76%) of stage III and 17 (77.3%) patients of stage IV, respectively. Overall percentage increase in levels of serum CEA from stage I through IV were 0%, 6.34%, 30.2%, 26% respectively. The sensitivity of serum CEA in our primary breast cancer (PBC) patients was 63.5%.

Conclusion: It is concluded that serum CEA had significant sensitivity in detecting breast cancer in our population. Elevated serum CEA levels were seen in various stages of our PBC patients.

Keywords: Carcinoembryonic antigen, Primary breast cancer.

INTRODUCTION

Tumor markers are gaining an important role in all aspects of cancer care, that includes screening and follow-up after treatment[1]. Their application in clinical practice needs knowledge of the basics of pathophysiology and techniques of their laboratory testing. The evidence of their role in any given malignancy needs to be incorporated in our clinical work. Tumor markers helps in screening, diagnosis and monitoring treatment leading to clinical decisions that are made based on their sampling results[1].

Serum CEA is a glycoprotein involved in cell adhesion. It is normally produced during fetal development and its production stops before birth. It is not usually found in the blood of healthy adults, although levels are raised in number of benign and malignant conditions and in heavy smokers as well.

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Received: 08 Dec 2015; revised received: 18 Jan 2016; accepted: 26 Jan 2016

The first description of tumor markers came from Egyptian papyrus and it dates back 2000 years ago, where a difference between breast cancer and mastitis was established. Bence Jones detected the first tumor marker in 1846, in samples of acidified urine from patients suffering from the disease "Mollities osseum". The first tumor antigen CEA was discovered by Gold et al in 1965, when he isolated a glycoprotein molecule from human colonic cancer specimen[2].

Tumor markers include a variety of substances like cell surface antigens, cytoplasmic proteins, enzymes, hormones, onco fetal antigens, receptors, oncogenes and their products. Their detection can be carried out either in tissue or in body fluids like ascitic fluid or pleural fluid and serum. The main properties of a tumor marker includes high specification to a particular tumor type, provides a lead-time over diagnosis/ screening and a high sensitivity to avoid false positive results. Additionally, the tests used for sampling the tumor marker should not be expensive enough for screening application at mass level.

Till todate, there are hundreds of tumor markers that have been used clinically in cancer management and among them serum CEA has been assessed in number of malignancies that includes breast, colorectum, stomach, pancreas, thyroid and lung[3]. The usefulness of serum CEA as diagnostic tool either alone or along with other tumor markers like HER 2 neu, CA 15[3] have also been studied in breast cancer patients[4]. The results have shown that serum CEA assays are helpful in screening, diagnostic confirmation, assessment of therapeutic response to treatment, monitoring disease and recurrences. However, diagnostic accuracy in malignant breast lesions was increased by combined assays with other tumor markers of breast carcinoma[5].

With this background, serum CEA levels assessments in our population can provide a helpful diagnostic tool for early detection of breast lesions. The objective of this study is to evaluate potential role of serum tumor marker CEA in diagnosis of malignant breast lesions in our population[4].

PATIENTS AND METHODS

This cross-sectional study was conducted between January 2014 to November 2014 at department of Oncology, Combined Military Hospital (CMH), Rawalpindi, Pakistan. The following criteria was used to enroll patients in the study.

Table-I: Clinical characteristics of the patients.

Characteristics (n)	No. of patients
Age (mean) (range)	47 (20-70)
Family history	
• Yes	15
• No	48
Nodal status	
• Node positive	53
• Node negative	10
Histopathology	
• IDCA	60
• ILCA	3
Grade	
• G1	2
• G2	32
• G3	29
Stage	
• I	2
• II	14
• III	25
• IV	22
CEA levels	
• Normal (< 5 ng/ml)	23 (36.5%)
• Raised (>5 ng/ml)	40 (63.5%)

CEA, carcinoembryonic antigen

Inclusion criteria

- Female gender.
- Patients with age ≥ 20 and ≤ 70 years.
- Patients with histopathologically confirmed carcinoma of breast.

Exclusion criteria

- Patients with more than one malignancy.
- Patients with history of smoking.
- Patients with other non-oncological conditions like endometriosis, pelvic

inflammation, hepatic cirrhosis, peptic ulcer, colitis and diverticulitis.

After getting approval from the Hospital Ethical Committee and informed consent, sixty three female patients from Oncology out patient department (OPD) and indoor patient department at CMH, Rawalpindi were enrolled by non-probability consecutive sampling. All patients were subjected to staging work-up that included physical examination, all base line investigations, serum biomarkers, radiological examinations including chest radiograph, ultrasound abdomen and pelvis, bone scan, CT scan / MRI of the chest (optional). Biopsy / surgery of the lesion revealed final histopathological diagnosis. Patients serum CEA levels were carried out only by blood sampling using chemiluminescent immunoassay with immulite 2000 CEA.

Data analysis were done with the help of the Statistical Package for the Social Sciences (SPSS) version 19 software. Mean and range was calculated for quantitative variable like age. Frequency and percentage was calculated for categorical variables like serum CEA. Value of serum CEA levels >2.5 ng / ml were taken as raised and ≤2.5ng / ml as normal. Chi-square test and Fisher's exact tests were applied for the association of CEA status stage and nodal status. A *p*-value <0.05 considered to be significant with value.

RESULTS

Sixty three female patients with histopathologically confirmed carcinoma of breast in our Oncology department revealed elevated serum CEA levels in three stages of the disease. The median age was 47 years (range, 20-70 years). Out of these 63 female patients, 15 (23.8%) patients had family history of the breast cancer. Invasive ductal carcinoma (IDCA) was the commonest histology with 60 (95.23%) patients and 3 (4.76%) patients were of invasive lobular carcinoma (ILCA) (table-I).

Table-II: Frequency of elevation of tumor marker Serum CEA with stage.

Stage grouping	CEA status		Total	*p*-value
	Normal	Raised		
Stage I	2	0	2	
Stage II	10	4	14	
Stage III	6	19	25	0.002
Stage IV	5	17	22	
Total	23	40	63	

CEA, carcinoembryonic antigen

Table-III: Frequency of elevation with nodal status.

Nodal status	CEA status		Total	*p*-value
	Normal	Raised		
Negative	8	2	10	
Positive	15	38	53	0.003
Total	23	40	63	

CEA, carcinoembryonic antigen

Among stage grouping, 2 (3.2%) patients had stage I disease, 14 (22.2%) had stage II, 25 (39.7%) had stage III and 22 (34.9%) patients had stage IV disease. Node positive cases were 53 (84.1%) and node negative were 10 (15.9%). Two (3.2%) patients were of grade 1 disease, 29 (50.8%) were of grade 2 and 29 (46%) patients were of grade 3 disease.

The frequency of abnormal CEA levels were varying from stage II to stage IV and with nodal status (table-II and III). Elevated serum CEA levels were noted in 0 (0%) patients of stage I, 4 (28.6%) of stage II, 19 (76%) of stage III and 17 (77.3%) patients of stage IV, respectively. Overall

percentage increase in levels of serum CEA from stage I through IV were 0%, 6.34%, 30.2%, 26% respectively. The sensitivity of serum CEA in our PBC patients was 63.5%.

DISCUSSION

CEA is one of the first tumour marker to be identified, and has been evaluated in number of malignancies including breast cancer[7-9]. The levels of serum CEA assay helps in diagnosis as well as prognosis in breast cancer patients. Several studies have shown that high levels of serum CEA reflects advanced stage of the disease in breast cancer patients[9]. The elevated levels of serum CEA are also associated with adverse outcomes[9].

The clinical use of tumor markers in breast cancer in our population is based on international data and guidelines. Therefore we studied serum CEA levels in our breast cancer population to evaluate its role in detecting breast cancer in our Pakistan population. No such study was carried out at our center before. Raised levels of serum CEA was observed in various stages of disease as shown in table-II. The sensitivity of serum CEA in our PBC patients was 63.5% (table-III).

Our results are consistent with results in international studies. In a study by Elfagiah et al increased levels of CEA were found in 62% of the breast cancer patients[4]. In another study by Hussain Gadelkarim Ahmed and Mohammed Omer M Hussein, frequency of elevated levels were seen in 60% of PBC patients[11].

In our study, serum levels of CEA were significantly associated with tumor burden i.e. advanced stage of the disease. The frequency of elevated CEA levels were higher in stage III and IV than in stage II, respectively (table-II). In a study by Porika et al elevated CEA levels were noted in stage III than in stage II and I (i.e. 7.1% in stage I, 28.6% in stage II, 64.3% in stage III patients, respectively)[5].

On the other hand, no significant association was found with levels of serum CEA and the patient's age, with 60% frequency of elevation in women aged from 20-40 years and 63.15% in age between 40-47 years. Similar findings have been documented by Park et al[11]. In contrast to this findings, Lumachi et al[12] reported correlation with the age of patients.

The potential limitations of our study are, one tumor marker was studied as CA 15-3 can also be used for detecting breast cancer alongwith CEA and sensitivity is even more with their combined assessment as evaluated in various international studies[5,10]. These tumor markers may have role in monitoring and prognosis of breast cancer alongwith diagnosis as revealed by various studies[13]. We have not performed the serum CEA level assessment after treatment to observe any fall in levels of serum CEA in order to moniter the efficacy of treatment as our study period was short. With longer follow up, sensitivity of serum CEA can be assessed more effectively.

CONCLUSION

It is concluded from our study that there was a significant sensitivity of tumor marker serum CEA in advanced stage of our breast cancer population. Evaluate serum CEA levels were seen in various stage of study PBC patients.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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