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SERUM BETA HCG LEVELS CORRELATION IN MALIGNANT BREAST LESIONS IN TERTIARY CENTRE OF SOUTHERN RAJASTHAN

General Surgery

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ABSTRACT

Introduction: Cancer of breast is the most common cancer affecting women worldwide and is the second most common cause of cancer death next to lung cancer. Based on the findings of this study, a potential for BETA HCG as a general breast disease marker, tumour marker, treatment option or prognostic factor can be assessed. **Objective:** This study aims at correlating serum BETA HCG level in carcinoma breast with TNM staging, various age groups and histological subtypes. **Method:** The study is a hospital based descriptive epidemiological study collecting data of BETA HCG in blood sample from patients diagnosed with carcinoma breast on tissue biopsy. **Results:** The study included 46 patients of carcinoma breast. While correlating BETA HCG with the size of the tumor, axillary nodal involvement and stage of disease, the p value is found to be <0.05.This shows strong association. Age and histopathlogical subtypes do not show any correlation with BETA HCG levels. Overall mean BETA HCG level was found to below normal. **Conclusion:** Even though BETA HCG cannot be used as tumour marker, its high significance with respect to TNM staging can be used to prognosticate the severity of breast carcinoma in women with palpable breast malignancies and to predict the outcome of the disease in association with other tumour markers such as ER, PR and HER2neu.

KEYWORDS

Beta Human Chorionic Gonadotropin (BETA HCG)

INTRODUCTION

Cancer of breast is the most common cancer affecting women worldwide and is the second most common cause of cancer death next to lung cancer.[1] Incidence of breast carcinoma is common in an urban Indian women as compared to rural women.

Beta Human Chorionic Gonadotropin is most commonly used for the detection of pregnancy. It is already a well-known fact that pregnancy is a protective factor against breast cancer. Some studies have also found that BETA HCG levels seem to be elevated in breast related lesions. The level of serum BETA HCG was found to be elevated in breast cancer because of upregulation in CGB 3-9 genes and a decrease in hCG receptor in cancer tissue.[2] This study focuses on the evaluation of BETA HCG in malignant breast lesions. BETA HCG is virtually undetectable in non-pregnant, healthy women. A value less than 5mIU/mL is considered to be normal.

Based on the findings of this study, a potential for BETA HCG as a general breast disease marker, tumor marker, treatment option or prognostic factor can be assessed. Depending on its sensitivity; which can be assessed in this study by evaluating the number of patients with malignant palpable breast lesion showing increased serum BETA HCG levels, its potential as a diagnostic test can be investigated. Furthermore, by looking closely at the trends in breast cancer, it can be assessed as a tool for staging of the cancer, patient prognosis or for the monitoring of treatment and individual progress.

MATERIALS AND METHODS

The patients were selected from hospitals in Udaipur affiliated to RNTMC.

Patients with malignant breast diseases presenting during approx. 1 year from institutional ethics committee approval time frame were selected.

1. Study Type: It was hospital based descriptive epidemiological study.

2. Study Design: Cross-sectional in design.

3. Study Area: Out patients/in patients –Department of general surgery, RNT Medical College, Udaipur.

4. Study Duration: Study was planned for approx. 1 year after institutional ethics committee approval.

5. Study Population: Patients with malignant breast lesions

6. Study Subjects: All patients presenting with breast disease of malignant variety.

Inclusion Criteria

- Patients giving consent
- Age group: 16 years and above
- Malignant breast lesion.

Exclusion Criteria

- Concurrent malignancy of any other organ such as ovarian cancer, choriocarcinoma and other BETA HCG secreting lesions.
- Age group of <16 years.
- Pregnancy and lactating women with malignant breast lesion.
- Not willing to give consent for participating in the study.
- Benign breast lesion.

7. Study Procedure:

Patients with malignant breast diseases presenting during approx. 1 year from institutional ethics committee approval time frame were selected.

Patient consent to participate in the study and patient's bystanders were thoroughly informed about the study and were assured that it would not affect their treatment in any way.

General physical examination and history was elicited from the patient prior to obtaining sample.

1. Patients with malignant breast lesions were selected according to the inclusion and exclusion criteria.
2. Blood was drawn from each patient to measure serum BETA HCG levels.
3. Data collected has been plotted in a graphical format to systematically observe the occurrence of BETA HCG in different disease entities.
4. Comparison of these levels according to different stages, histological type and age is done.

Interpretation Of Values

- BCF β-hCG values are compared with the standard reference serum βhCG value (Normal reference value of Serum β-hCG <5mlU/L.
- Any BCF β-hCG value greater than 5 mIU/mL is considered increased value and those less than 5 mIU/mL are considered not significant.

Several comparisons were thus be generated in terms of:

- Difference in BETA HCG levels in the different histological types of breast cancer.

- Difference in levels according to stage of disease, size of tumor and axillary lymph node status.
- Differences according to age of the patient

8. Data Analysis

Statistical analysis of the data obtained was done using student's unpaired t' test and chi square test. A statistical package SPSS version 17.0 will be used to do the analysis. A 'p' value of <0.05 will be taken as significant.

Observations

In our study of 46 patients, the age of females was in the range of 26 to 80 years, with majority belonging to age group .50 years (60.81. The mean age of presentation was 53.39. Out of 46 cases, 22(47.8%) had lump in left breast and 24(52.17%) had lump on right side. Maximum number of cases presented between 6-12 months after the onset of symptoms (n=23, 50%). Out of 46 patients, 11 had positive family history of carcinoma breast. Patient's mother or grandmother had similar complaints and relevant history of carcinoma breast was elicited.

Table 1: Correlating BETA HCG with the stage of the tumor

			Serum BETA HCG level			total
			<2.5	2.5-5	>5	
Stage	1	Count	1	0	0	1
		%	7.1%	.0%	.0%	2.2%
	2	Count	8	6	0	14
		%	57.1%	26.1%	.0%	30.4%
	3	Count	5	15	4	24
		%	35.7%	65.2%	44.4%	52.2%
	4	Count	0	2	5	7
		%	0%	8.7%	55.6%	15.2%
Total		Count	14	23	9	46
		%	100.0%	100.0%	100.0%	100.0%

	Value	df	P
Pearson Chi-Square	22.426a	6	.001

While correlating BETA HCG with the stage of the tumor, the p value is 0.001. This shows strong association of BETA HCG with the stage of tumor especially with stage (52.2%).

Table 2: Correlating BETA HCG with the size of the tumor

			Serum BETA HCG level (IU/mL)			Total
			<2.5	2.5-5	>5	
T stage	1 Till 2cm	Count	3	0	1	4
		%	21.4%	.0%	11.1%	8.7%
	2 2-5cm	Count	7	4	1	12
		%	50.0%	17.4%	11.1%	26.1%
	3 >5cm	Count	4	16	0	20
		%	28.6%	69.6%	.0%	43.5%
	4 Chest wall invol.	Count	0	3	7	10
		%	.0%	13.0%	77.8%	21.7%
Total		Count	14	23	9	46
		%	100.0%	100.0%	100.0%	100.0%

	Value	df	P
Pearson Chi-Square	34.253a	6	.000

While correlating BETA HCG with the size of the tumor, the p value is 0.000. This shows strong association of BETA HCG with the size of tumor especially with tumor size >5cm.

Table no.3 correlating BETA HCG with nodal stage.

			SERUM BETA HCG LEVELS			Total
			<2.5	2.5-5	>5	
N stage	0	Count	8	3	1	12
		%	57.1%	13.0%	11.1%	26.1%
	1	Count	3	13	2	18
		%	21.4%	56.5%	22.2%	39.1%
	2	Count	3	6	6	15
		%	21.4%	26.1%	66.7%	32.6%
	3	Count	0	1	0	1
		%	.0%	4.3%	.0%	2.2%
Total		Count	14	23	9	46
		%	100.0%	100.0%	100.0%	100.0%

	Value	df	P
Pearson Chi-Square	16.044a	6	.014

In this study the axillary nodal status was studied and correlated with the BETA HCG while correlating the p value was found to be 0.014, which show positive association.

DISCUSSION

Tumour size status in Carcinoma Breast and correlation with BETA HCG Size of the tumor is important in carcinoma breast as tumor size determines the stage of disease and is of prognostic value. In our study tumor size and serum BETA HCG level were correlated. In this study, twenty cases (43.47%) had tumor with greatest diameter more than 5cms. Out of the 46 cases, ten (21.73%) had tumor with direct extension to the chest wall and to the skin. This is comparable to talha et al 39.5% cases had size > 5 cms. . In vasudevan et al(2), 58.7% patients had T2, as compared to30.4% of our study .This shows lack of awareness and ignorance, leading to late presentation of the disease in our study.

The serum BETA HCG level showed a rising trend with progression in the stage of the disease; that is, as the T stage worsened. There was also a direct correlation noted between the T stage of the disease and BETA HCG, with increased levels of serum BETA HCG with a p value of 0.001 which is highly significant and similar results were obtained in talha et al with p value of 0.016. Vasuedevan et al (2) reported maximum rise in BETA HCG in T3 stage.

Axillary lymph node status in Carcinoma Breast and correlation with BETA HCG

In our study, 73.87% cases had histopathologically positive lymph nodes, 32.60% cases had N2 stage and 39.10% cases had N1. Lymph node negative status was observed in the remaining 26.08% cases. Talha et al (3) 21.5% had N2 stage, and 30.5% had N1 stage. In Vasudevan et al, 45.3% patients had no nodal involvement. 25% and 21% patients belonged to N1 and N2 stages respectively .This shows advanced disease and late presentation because of shyness, ignorance, illiteracy and lack of awareness in our study.

BETA HCG level was also found to correlate with the N stage, with a rise seen in serum BETA HCG value with a progressing N stage of the disease .

Stage at presentation in carcinoma breast and correlation with BETA HCG In the present study there were 52.17% cases belonged to stage III. Which is in accordance with the study of vasudevan et al (2), 48% patients belonged to TNM stage 3. While talha et al reported maximum cases in stage II (43.0%). In our study, the maximum numbers of patients were among TNM stage III.

The p value for BETA HCG was found to have significance association with the stage of the disease, with respect to TNM classification of breast carcinoma, with a p value of 0.0001. Similar results were obtained in talha et al with p value of 0.000. Vasudevan et al (2) had the similar result showing direct correlation of BETA HCG level and stage of carcinoma breast with value of 0.018.

While a study by Agnantis NJ, et al,(3) showed that certain histopathological subtypes stained positively for the beta subunit of HCG using immunoperoxidase technique; our study, in spite of encompassing the major histopathological subtypes of carcinoma breast did not show any association between value of serum BETA HCG and the histological subtype of carcinoma

A study by Schüler-Toprak S, et al (4), seems to point firmly at the expression of BETA HCG on breast cells during malignancy of the breast, but our study contradicts these findings

RESULTS

All the patients evaluated were also subjected to a histopathological diagnosis with a metastatic workup and a TNM staging. Amongst the 46 women evaluated, the p value for BETA HCG was found to have significance association with the stage of the disease, with respect to TNM classification of breast carcinoma, with a p value of 0.0001. The serum BETA HCG level showed a rising trend with progression in the stage of the disease; that is, as the stage worsened. There was also a positive correlation noted between the T stage of the disease and BETA HCG, and with a p value of 0.001 which is highly significant. It was

also found to correlate with the N stage, with a rise seen in serum BETA HCG value with a progressing N stage of the disease. Similar findings were also observed in Stage 3 and Stage 4 of breast carcinoma, with increased levels of serum BETA HCG. There was no direct correlation noted between the metastases of the disease. Evaluation of BETA HCG levels in blood is a faster, cost effective and easy to execute method as compared to the detection of other tumour markers and hence can be used to assess the prognosis in patients.

In our study, serum BETA HCG levels were not found to have an association with the histological type of breast carcinoma, leading to the inference that changes in BETA HCG values were independent of the histological subtype. Similarly, there was no correlation observed between BETA HCG levels and age of the patient with breast carcinoma. Even though BETA HCG cannot be used as tumour marker, its high significance with respect to TNM staging can be used to prognosticate the severity of breast carcinoma in women with palpable breast malignancies and to predict the outcome of the disease in association with other tumour markers such as ER, PR and HER2neu.

CONCLUSION

In our study, serum BETA HCG level were studied in histologically diagnosed patients of carcinoma breast. Overall, the mean BETA HCG level was found to be less than normal. While establishing trends, positive correlation was found between BETA HCG and stage of disease, size and axillary lymph node status no correlation was found between in histopathology of tumor and age of patient.

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