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Research Article

Post-treatment alterations of serum cancer antigen 125, cancer antigen 19.9 and carcinoembryonic antigen levels in patients with gynecological malignancies in a tertiary care hospital in eastern India

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ABSTRACT

Background: Gynecological carcinomas form a significant proportion of all malignancies in women across the globe. These are associated with an increase in the serum concentrations of certain tumor markers such as cancer antigen (CA)125, CA19.9 and carcinoembryonic antigen (CEA) that correlate with the tumor burden.
Methods: Pre- and post-treatment serum levels of CA125, CA19.9 and CEA were determined in 36 patients of ovarian carcinoma, 31 patients of cervical carcinoma and 20 patients of endometrial carcinoma using enzyme-linked immunosorbent assay. The pre- and the post-treatment levels of these markers have been compared and correlated.
Results: With primary treatment, CA125 level was significantly reduced in ovarian, endometrial (ps < 0.001) and cervical (p = 0.001) carcinomas and that of CA19.9 was significantly decreased in cervical and endometrial carcinomas (ps < 0.001). Surprisingly, post-treatment CEA level was significantly increased in cervical carcinoma (p = 0.001) with significant increase after radiotherapy (p = 0.003), but not after surgery (p = 0.091). Treatment had no effects on CA19.9 level in ovarian carcinoma and on CEA levels in ovarian and endometrial carcinomas. Pre- and post-treatment levels of CA125, CA19.9 and CEA showed strong positive correlation in cervical carcinoma, while those of CA19.9 showed very strong positive correlation in endometrial carcinoma.
Conclusions: Post-treatment serum CA125 level best reflects the treatment effect in all three types of gynecological carcinomas. CA19.9 is reliable to evaluate treatment effect in patients of cervical and endometrial carcinomas. Studies involving larger population size should be conducted to identify the changes in CEA while assessing treatment effect in cervical carcinoma patients.

Keywords: Cancer antigen 125, Cancer antigen 19.9, Carcinoembryonic antigen, Gynecological carcinoma, Enzyme-linked immunosorbent assay

INTRODUCTION

Gynecological malignancies constitute 10-15% of all the new cases of cancers detected every year in India.[1] From 1985 to 1999, this group comprised 42.52% of all malignancies in Indian women.[2] In India, about 50-60% of all cancers among women occur mainly in the cervix uteri, breast, corpus uteri and ovaries.[1] More than 80% cervical cancer cases occur in the developing countries[3,4] while almost 60% of corpus uteri cases have been reported to occur in the developed world.[4] In the United States, endometrial cancers are more common than cervical cancers.[5] In Indian

scenario, the deadliest gynecological cancer is the ovarian cancer, which is detected in an advanced stage in two-third of the cases.[1] Clinico-pathological screening along with early interventions vouch for a better prognosis in these conditions.

Certain tumor markers or biomarkers have revolutionized screening, risk stratification and follow up in gynecological oncology. The carbohydrate antigen Sialyl Lewis a, also known as cancer antigen (CA)19.9,[6] has been described as the most homogeneously distributed marker of almost all endometrial carcinoma samples making it a possible useful marker for endometrial carcinoma.[7] CA125 is a high molecular weight glycoprotein antigenic determinant with a role in monitoring treatment and detecting recurrence of ovarian cancer and is a prognostic marker for advanced ovarian cancer.[8] Although elevated mainly in ovarian cancers (82%), CA125 is also raised in various non-ovarian and non-gynecologic malignancies as well as in various inflammatory and non-malignant conditions.[9,10] However, as per the National Academy of Clinical Biochemistry (NACB) guidelines, CA125 has been stated as the only tumor marker that has been accepted for clinical use in ovarian cancer.[11] Carcinoembryonic antigen (CEA) is a glycoprotein present in elevated levels in both gynecological and non-gynecological disorders.[10,12] Although the pre-treatment serum levels of these tumor markers have been vividly studied previously to evaluate their prognostic capabilities,[13] very few have actually looked into the treatment effect of their serum levels. Hence, in the present study, rather than evaluating the elevated serum levels, we have tried to correlate the pre-treatment serum levels of these three tumor markers individually with their post-treatment levels, thereby evaluating the effects of the treatment on the serum levels of the markers.

METHODS

Study population

The study was approved by the Institutional Ethics Committee, which follows the guidelines set by the Declaration of Helsinki for biomedical research. Informed consents from the patients or their close relatives were obtained prior to the start of the study. The study was performed in the Department of Biochemistry and Department of Obstetrics and Gynecology over a period of 18 months. Newly diagnosed cases of invasive cervical carcinoma (confirmed by the combination of clinical examination and cervical histopathological features), ovarian carcinoma (confirmed by the combination of clinical features, ultrasonographic features, and histopathological features of ultrasonography - or computerized tomography - guided biopsy), and endometrial carcinoma (confirmed by the combination of clinical features, ultrasonography and histopathological features of endometrial biopsy) admitted to the Department of Obstetrics and Gynecology were included in the study. International Federation of Gynecology and Obstetrics (FIGO) surgical staging of all the carcinomas were done during laparotomy. Patients with dysfunctional uterine bleeding, benign ovarian cyst, cervical erosion, human papilloma virus infection, low-grade squamous intraepithelial lesion, high-grade squamous intraepithelial lesion, genital tuberculosis, pregnancy and/or already receiving therapeutic intervention for malignancy were excluded from the study. Individual case history with pathological findings was noted down with the help of well-designed case record proforma. A total of 87 cases (36 patients of ovarian carcinoma, 31 patients of cervical carcinoma and 20 patients of endometrial carcinoma) fulfilling all the above-mentioned criteria were included in the study. Five weeks after treatment, patients were evaluated to assess for any signs or symptoms of recurrence of the diseases.

Therapeutic interventions

Each malignancy was assigned an FIGO stage and pre-treatment serum levels of CEA, CA125 and CA19.9 were measured (as described in the methods section). According to FIGO stages and clinical conditions, patients were assigned to receive primary treatment either by surgery, radiotherapy or chemotherapy, singly or in combination, following the National Comprehensive Cancer Network guidelines. Accordingly, following modes of treatment were done: (a) Ovarian carcinoma: Total abdiminal hysterectomy with bilateral salpingo-oophorectomy with comprehensive staging or unilateral salpingo-oophorectomy (USO; clinical stage IA or IC, all grades with comprehensive staging if patient desired fertility) or cytoreductive surgery for clinical stage II, III or IV, or neoadjuvant chemotherapy (category 1) or primary interval cytoreduction for patients with bulky stage III/IV who were poor surgical candidates due to high-risk comorbid conditions or disease factors were performed. (b) Cervical carcinoma: Patients with cervical cancer in the study underwent radical Wertheim's hysterectomy or primary radiotherapy (85-90 Gy delivered to point A and 60 Gy to point B) as per the clinical stages of the disease.[14,15] (c) Endometrial carcinoma: Patients with endometrial cancer underwent either extra-fascial hysterectomy or primary radiotherapy.

Sample collection

A volume of 5 ml fasting venous blood was collected aseptically in separately labeled sterile clot-retraction vials and left to stand for 30 min at room temperature. The samples were then centrifuged at 1500 rpm for 10 min and sera collected in correspondingly labeled micro-centrifuge tubes (Eppendorf, India) and kept at −20°C. They were analyzed for CEA, CA125 and CA19.9 levels within 20 days of storage, which is well within the time-frame recommended in the NACB guidelines.

Estimation of serum levels of the tumor markers

The pre-treatment (7 days prior to therapy) and post-treatment (5 weeks after therapy) serum levels of CEA, CA125 and CA19.9 levels were estimated by sandwich enzyme-linked immunosorbent assay (ELISA) using

Accubind kit (Monobind Inc., California, USA) following the manufacturer's protocol. Briefly, calibrators, sera, and controls were added to the respective wells of the streptavidin-coated microplate followed by the addition of the corresponding biotinylated monoclonal antibodies. After the immune complex formed by the antigen-antibody reaction bound to the streptavidin coated to the wells, the unbound proteins of the samples were washed with wash solution containing a surfactant in buffered saline. Another enzyme-labeled antibody to a specific antigen (CEA, CA125 or CA19.9) was added to the wells that bound to the antigen immobilized on the walls by the biotinylated monoclonal antibody already on the wall. Excess enzyme was washed away followed by addition of tetramethylbenzidine in hydrogen peroxide and acetate buffer. Stop solution was added followed by measurement of absorbance at 450 nm in a microplate reader. Subtracting the blank absorbance from that of the samples gave the concentration of the antigen in the serum from the standard concentration-absorbance curve drawn with the known concentrations of the antigens. The validity of the tests was monitored by the quality control parameters following the manufacturer's protocol. Each sample was tested in duplicate wells, and their mean absorbance value was taken for analysis.

Statistical analyses

Comparison of the change in tumor marker levels with treatment was done for every malignancy using the Wilcoxon's matched-pairs signed-rank test. Correlation between tumor marker levels before and after treatment was quantified by Spearman's rank correlation coefficient. Magnitude of Spearman's correlation coefficient (r_s) was interpreted as described previously.[16] Briefly, r_s between 0.9-1.0 was considered very strong, 0.7-0.9 was strong, 0.5-0.7 was moderate, 0.3-0.5 was low, and 0.0-0.3 was negligible correlation. A value of $p < 0.05$ was considered as statistically significant. Values were expressed as (mean ± standard error of mean) in the figures, as (mean ± standard deviation) and (mean [interquartile range]) in the tables, or as percentages. Statistical analyses were done using Microsoft Excel, Statistica (StatSoft Inc., Tulsa, Oklahoma, USA) and GraphPad Prism (GraphPad Software Inc., San Diego, California, USA) software.

RESULTS

Distribution of the different carcinomas among the study population

Table 1 shows the distribution of the number of ovarian, cervical and endometrial carcinomas in different stages (Stage I-IV) among the study population. 36/87 (41.38%) were affected by ovarian carcinoma, 31/87 (35.63%) were affected by cervical carcinoma and 20/87 (22.99%) were affected by endometrial carcinoma. Of the different carcinoma stages, the most common was Stage I cervical carcinoma (35.48%), followed by Stage III ovarian carcinoma (30.56%); whereas the least common was Stage IV endometrial carcinoma (5%). Table 2 shows the distribution of the different histological subtypes of the malignancies. Papillary serous adenocarcinoma was found to be the most common histological variant (58.33%) among the ovarian carcinomas. Well-differentiated squamous cell carcinoma was found to be the most common histological subtype in cervical carcinoma (58.06%) while well-differentiated endometroid adenocarcinoma was the most common histological subtype in endometrial carcinoma (55%).

Pre- and post-treatment levels of the tumor markers

Serum CA125

The pre-treatment CA125 levels (U/mL) in patients of ovarian carcinoma, cervical carcinoma and endometrial carcinoma were 377.02 ± 514.50, 41.39 ± 39.51 and 77.14 ± 69.50 respectively, while the post-treatment levels were 83.38 ± 141.05, 28.64 ± 29.75 and 38.13 ± 24.75 respectively. There was significant decrease of the post-treatment levels of CA125 in all the three cases of carcinomas (ps < 0.001, $= 0.001$, < 0.001 respectively) (Figures 1a, 2a and 3a; Table 3).

Serum CA19.9

The pre-treatment CA19.9 levels (U/mL) in patients of ovarian carcinoma, cervical carcinoma and endometrial carcinoma were 34.57 ± 98.55, 35.54 ± 26.53 and 20.45 ± 16.00 respectively, while the post-treatment levels were 23.55 ± 23.64, 27.56 ± 22.49 and 12.39 ± 9.73 respectively. There was significant decrease of the post-treatment levels of CA19.9 in cervical carcinoma and endometrial carcinoma cases only ($p < 0.001$ in both cases) but no significant change in ovarian carcinoma ($p = 0.912$) (Figures 1b, 2b and 3b; Table 4).

Serum CEA

The pre-treatment CEA levels (ng/mL) in patients of ovarian carcinoma, cervical carcinoma and endometrial carcinoma were 3.44 ± 5.00, 7.01 ± 11.36 and 2.29 ± 2.33 respectively, while the post-treatment levels were 3.04 ± 1.99, 8.97 ± 11.45 and 2.53 ± 1.45 respectively. There was significant increase of the post-treatment levels of CEA only in cervical carcinoma cases ($p = 0.001$) but not in ovarian carcinoma ($p = 0.765$) and endometrium ($p = 0.433$) (Figures 1c, 2c and 3c; Table 5).

Correlation between pre- and post-treatment tumor marker levels in the different carcinomas

There was a low positive correlation of the CA125 ($r_s = 0.37$, $p < 0.05$) levels and a moderate positive correlation of the CA19.9 ($r_s = 0.57$, $p < 0.001$) levels before and after treatment of ovarian carcinoma (Figures 1d and e) but negligible correlation of the CEA levels in ovarian carcinoma ($r_s = 0.13$, $p < 0.05$) (Figure 1f). In case of cervical carcinoma,

Table 1: Distribution of the stages of different types of gynecological malignancies and the age-groups of the patients.

	Age (years)	Number of patients (%)			
		Stage I	Stage II	Stage III	Stage IV
Ovarian carcinoma, *n*=36 (41.38%)	45.2±10.98	6 (16.67)	10 (27.78)	11 (30.56)	9 (25)
Cervical carcinoma, *n*=31 (35.63%)	52.7±10.72	11 (35.48)	9 (29.03)	8 (25.81)	3 (9.68)
Endometrial carcinoma, *n*=20 (22.99%)	57.5±7.21	7 (35)	7 (35)	5 (25)	1 (5)

Age values presented as mean±standard deviation

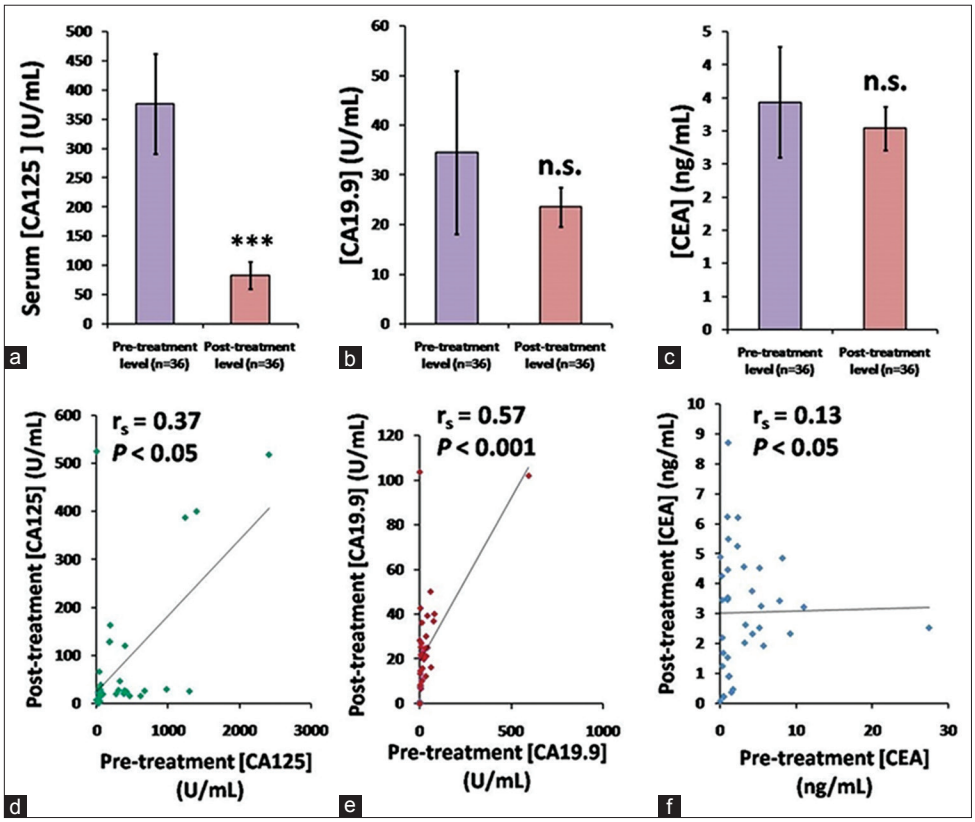

Figure 1: Serum levels of tumor markers in patients of ovarian carcinoma: (a) Significant reduction of serum cancer antigen (CA)125 levels occurs after treatment. CA125 levels were measured by enzyme-linked immunosorbent assay (ELISA). Values represented as mean ± standard error of mean (SEM). Comparison done by Wilcoxon's matched pairs signed-rank tests. (b) No significant reduction of serum CA19.9 levels occurs after treatment. CA19.9 levels were measured by ELISA. Values represented as mean ± SEM. Comparison done by Wilcoxon's matched pairs signed-rank tests. (c) No significant reduction of serum carcinoembryonic antigen (CEA) levels occurs after treatment. CEA levels were measured by ELISA. Values represented as mean ± SEM. Comparison done by Wilcoxon's matched pairs signed-rank tests. (d) Spearman's rank correlation test reveals a low positive correlation ($r_s = 0.37$, $p < 0.05$) between the pre- and the post-treatment levels of CA125. (e) Spearman's rank correlation test reveals a moderate positive correlation of the CA19.9 ($r_s = 0.57$, $p < 0.001$) between the pre- and the post-treatment levels of CA19.9. (f) A negligible correlation ($r_s = 0.13$, $p < 0.05$) exists between the pre- and the post-treatment levels of CEA. ***$p < 0.001$, n.s.: No significant difference.

there were high (strong) positive correlation of the CA125 ($r_s = 0.85$, $p < 0.001$), CA19.9 ($r_s = 0.87$, $p < 0.001$) and CEA ($r_s = 0.71$, $p < 0.001$) levels before and after treatment (Figures 2d-f). There was a moderate positive correlation of CA125 ($r_s = 0.62$, $p < 0.01$) and a very high (very strong) positive correlation of the CA19.9 ($r_s = 0.91$, $p < 0.001$) levels before and after treatment of endometrial carcinoma (Figure 3d and e) but negligible correlation of the CEA levels in endometrial carcinoma ($r_s = 0.26$, $p < 0.05$) (Figure 3f).

Changes in tumor marker levels with mode of treatment of the carcinomas

The reduction in levels of CA125 which occurred after surgery ($p = 0.002$) and chemotherapy ($p < 0.001$) of ovarian carcinomas were statistically significant, while there was no significant change in CA19.9 (surgery $p = 0.30$, chemotherapy $p = 0.23$) and CEA (surgery $p = 0.28$, chemotherapy $p = 0.12$) levels after treatment (Figures 1a-c).

Table 2: Distribution of the histological subtypes of the carcinomas.

Carcinoma types	Histological subtypes	Number of cases (% of the type)
Ovarian carcinoma		36
	Papillary serous adenocarcinoma	21 (58.33)
	Malignant mucinous carcinomas	6 (16.67)
	Poorly differentiated serous adenocarcinomas	9 (25)
Cervical carcinoma		31
	Well-differentiated squamous	18 (58.06)
	Moderately differentiated squamous	1 (3.23)
	Poorly differentiated squamous	11 (35.48)
	Papillary adenocarcinoma	1 (3.23)
Endometrial carcinoma		20
	Well-differentiated endometrioid adenocarcinoma	11 (55)
	Poorly differentiated adenocarcinoma	5 (25)
	Papillary serous carcinoma	3 (15)
	Adenosquamous variant of endometrioid carcinoma	1 (5)

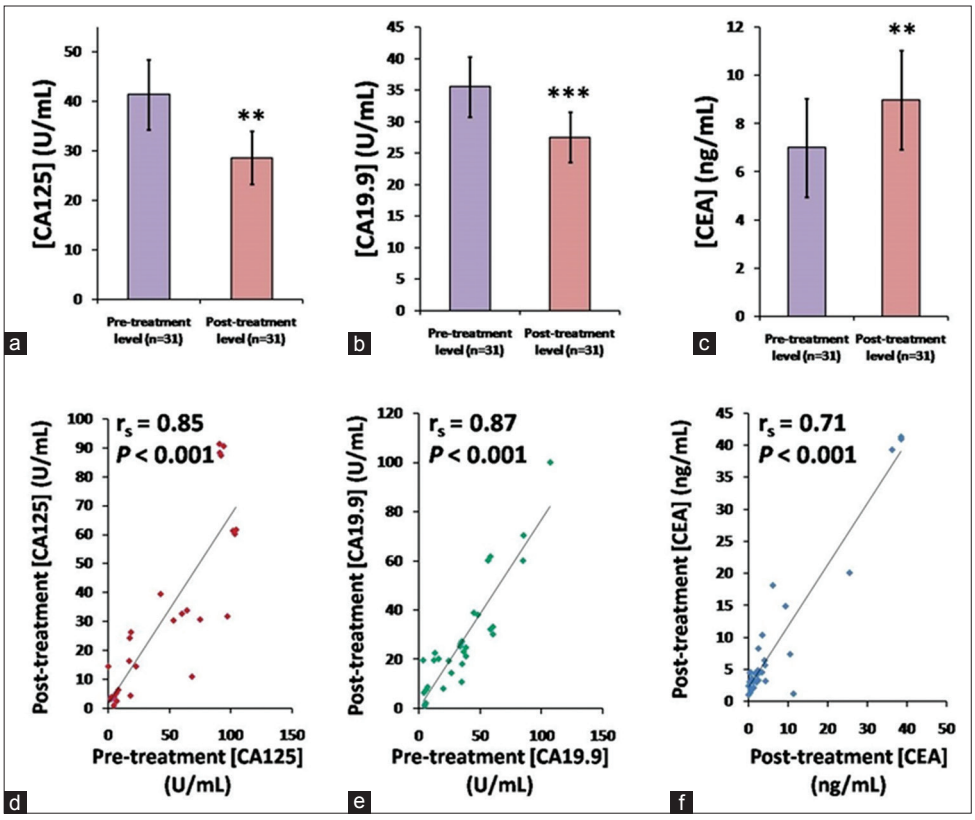

Figure 2: Serum levels of tumor markers in patients of cervical carcinoma: (a) Significant reduction of serum cancer antigen (CA)125 levels occurs after treatment. CA125 levels were measured by enzyme-linked immunosorbent assay (ELISA). Values represented as mean ± standard error of mean (SEM). Comparison done by Wilcoxon's matched pairs signed-rank tests. (b) Significant reduction of serum CA19.9 levels occurs after treatment. CA19.9 levels were measured by ELISA. Values represented as mean ± SEM. Comparison done by Wilcoxon's matched pairs signed-rank tests. (c) Significant increase of serum carcinoembryonic antigen (CEA) levels occurs after treatment. CEA levels were measured by ELISA. Values represented as mean ± SEM. Comparison done by Wilcoxon's matched pairs signed-rank tests. (d) Spearman's rank correlation test reveals a high (strong) positive correlation ($r_s = 0.85$, $p < 0.001$) between the pre- and the post-treatment levels of CA125. (e) A high (strong) positive correlation ($r_s = 0.87$, $p < 0.001$) exists between the pre- and the post-treatment levels of CA19.9. (f) Spearman's rank correlation test reveals a high (strong) positive correlation ($r_s = 0.71$, $p < 0.001$) between the pre- and the post-treatment levels of CEA. **$p < 0.01$; ***$p<0.001$.

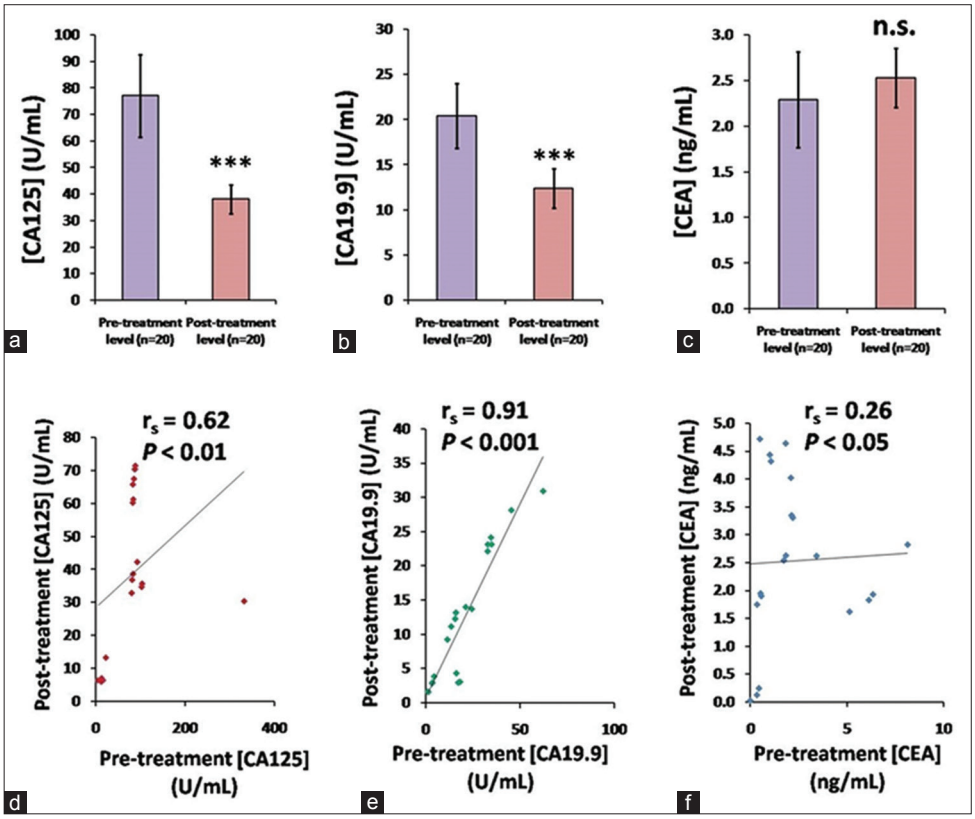

Figure 3: Serum levels of tumor markers in patients of endometrial carcinoma: (a) Significant reduction of serum cancer antigen (CA) 125 levels occurs after treatment. CA125 levels were measured by enzyme-linked immunosorbent assay (ELISA). Values represented as mean ± standard error of mean (SEM). Comparison done by Wilcoxon's matched pairs signed-rank tests. (b) Significant reduction of serum CA19.9 levels occurs after treatment. CA19.9 levels were measured by ELISA. Values represented as mean ± SEM. Comparison done by Wilcoxon's matched pairs signed-rank tests. (c) No significant change of serum carcinoembryonic antigen (CEA) levels occurs after treatment. CEA levels were measured by ELISA. Values represented as mean ± SEM. Comparison done by Wilcoxon's matched pairs signed-rank tests. (d) Spearman's rank correlation test shows a moderate positive correlation ($r_s = 0.62$, $p < 0.01$) between the pre- and the post-treatment levels of CA125. (e) Spearman's rank correlation test reveals a very high (very strong) positive correlation ($r_s = 0.91$, $p < 0.001$) between the pre- and the post-treatment levels of CA19.9. (f) A negligible correlation ($r_s = 0.26$, $p < 0.05$) exists between the pre- and the post-treatment levels of CEA. ***$p < 0.001$, n.s.: No significant difference.

Table 3: Changes in CA125 levels with treatment.

Carcinoma types	CA125 level (U/mL)		
	Mean±SD	Median (IQR)	*p* value
Ovarian carcinoma			
Pre-treatment	377.02±514.50	189.83 (43-410)	<0.001
Post-treatment	83.38±141.05	25.65 (17-56)	
Cervical carcinoma			
Pre-treatment	41.39±39.51	18.53 (4.80-90)	0.001
Post-treatment	28.64±29.75	16.25 (3.90-39.41)	
Endometrial carcinoma			
Pre-treatment	77.14±69.50	82.65 (18-87)	<0.001
Post-treatment	38.13±24.75	36.22 (10-63)	

SD: Standard deviation, IQR: Interquartile range, CA: Cancer antigen

The reduction in levels of CA125 ($p < 0.001$) and CA19.9 ($p = 0.003$) which occurred after primary surgery of cervical carcinoma were statistically significant (Figures 2a and b; Table 6). The reduction in the levels of CA125 ($p < 0.001$) and CA19.9 ($p < 0.001$) which occurred after primary surgery of endometrial carcinoma was statistically

Table 4: Changes in CA19.9 levels with treatment.

Carcinoma type	CA19.9 level (U/mL)		
	Mean±SD	Median (IQR)	*p* value
Ovarian carcinoma			
Pre-treatment	34.57±98.55	9.04 (2.60-34.1)	0.912
Post-treatment	23.55±23.64	20.46 (8.40-29.30)	
Cervical carcinoma			
Pre-treatment	35.54±26.53	35.01 (12.60-6.41)	<0.001
Post-treatment	27.56±22.49	22.61 (10.84-33.23)	
Endometrial carcinoma			
Pre-treatment	20.45±16.00	16.64 (7.90-32)	<0.001
Post-treatment	12.39±9.73	11.68 (2.90-22.60)	

SD: Standard deviation, IQR: Interquartile range, CA: Cancer antigen

Table 5: Changes in CEA levels with treatment.

Carcinoma type	CEA level (ng/mL)		
	Mean±SD	Median (IQR)	*p* value
Ovarian carcinoma			
Pre-treatment	3.44±5.00	1.37 (0.75-4.70)	0.765
Post-treatment	3.04±1.99	2.91 (1.56-4.50)	
Cervical carcinoma			
Pre-treatment	7.01±11.36	2.35 (0.81-6.12)	0.001
Post-treatment	8.97±11.45	4.52 (3.11-8.32)	
Endometrial carcinoma			
Pre-treatment	2.29±2.33	1.78 (0.51-2.80)	0.433
Post-treatment	2.53±1.45	2.57 (1.7-3.60)	

SD: Standard deviation, IQR: Interquartile range, CEA: Carcinoembryonic antigen

Table 6: Comparison of change in tumor marker levels with mode of treatment.

Carcinoma type	Mode of therapy	*p* values (pre- vs. post-treatment serum levels)		
		CA 125	CA 19.9	CEA
Ovarian	Surgery	0.002	0.304	0.284
Ovarian	Chemotherapy	<0.001	0.229	0.119
Endometrial	Surgery	<0.001	<0.001	0.854
Cervical	Surgery	<0.001	0.003	0.091
Cervical	Radiotherapy	0.431	0.080	0.003

CEA: Carcinoembryonic antigen, CA: Cancer antigen

significant, but there was no significant change in CEA ($p = 0.85$) after surgery (Figures 3a-c; Table 6). However, there was a statistically significant increase in levels of CEA after radiotherapy in cervical carcinoma patients ($p = 0.003$), but no significant change in its level was observed after surgery ($p = 0.091$) (Table 6). There was an overall effect of increase in CEA level after radiotherapy in cervical carcinoma patients (Figure 2c).

DISCUSSION

In this study, we have used a prospective non-randomized study design to observe the treatment effects on the changes of serum levels of three tumor markers (CA125, CA19.9 and CEA) in three common gynecological malignancies (ovarian, cervical, and endometrial). Previous studies point out the direct relation between the levels of the tumor markers and the gynecological tumor burden (tumor antigen concentration x extent of disease)[17] and hence, evaluating the alterations of the markers may help to infer about the effect of the treatment modalities in reducing the respective tumor burden.

In the present study population, ovarian carcinoma is the most common gynecological malignancy (~41%). Surgery and chemotherapy are effective in reducing the serum CA125 levels significantly in this group of patients. CA19.9 and CEA do not appear to be related with ovarian tumor burden since there is no significant change of their serum levels after treatment. These findings suggest that CA125 is the most appropriate marker of ovarian carcinoma that reflects the tumor burden. This fact is supported by one previous study where the level of CA125 correlated well with the tumor load in epithelial ovarian cancer.[18] CA125 is

a very useful parameter for monitoring response of ovarian carcinoma to chemotherapy.[19] As per the NACB guidelines, after primary therapy, monitoring of CA125 levels in women along with a routine history and physical and rectovaginal pelvic examination, has been suggested instead of surgery for asymptomatic women.[11]

Surgery, but not radiotherapy, is effective in reducing CA125 and CA19.9 levels in cervical carcinoma, which constitute the second most common group of gynecological malignancy in our study population (~36%). There is a strong positive correlation between their pre- and post-treatment serum levels as well, indicating that higher pre-treatment levels are associated with higher post-treatment serum levels, although the latter is expected to be reduced than the former (Figure 1). Serum CEA levels show a paradoxical significant elevation in the post-treatment conditions. Although this phenomenon can be ascribed to either relapse or recurrence of the carcinoma, we did not find such features in any patients. Hence, it has become difficult to assign specific reason for such observation. These cases definitely warrant further scrutiny with periodic follow-up with clinical and laboratory examinations.

Surgery is effective in reducing the serum levels of CA125 and CA19.9 in endometrial carcinomas in our study population. However, serum levels of CEA does not show any significant difference between the pre- and the post-treatment groups of endometrial carcinoma, indicating that the reduction of the tumor burden is not related to CEA level. There is also moderate to strong positive correlation between the pre- and the post-treatment levels of CA125 and CA19.9 in the group of patients with endometrial carcinoma. In support of our finding that CA19.9 is a useful marker in endometrial carcinoma, there has been a previous report where it has been found to be homogeneously distributed in all endometrium samples studied.[7] Another study supports our finding that CA125 is a useful biochemical tool for post-treatment monitoring of patients with endometrial carcinomas.[19] A moderate yet significant positive correlation between the FIGO scores and the serum CA125 levels exists (data not shown) indicating that CA125 level is a good predictor of the disease progression compared to the other two serum markers. In support of this finding, there are reports of many trials which have established the prognostic value of the rate of decrease in CA125 after cytoreductive surgery and during cytotoxic chemotherapy, and some guidelines recommend its prognostic use.[20]

Limitations of the study

Although the correlation between the pre- and the post-treatment serum levels of certain tumor markers in gynecological malignancies have been found, there are a few inherent limitations of this study. We have measured the tumor marker levels in the serum only once (although in duplicate) before and after the treatment, but it is more appropriate to measure them at least on two separate occasions to confirm that it is a consistent value and not a transient one. Although the novelty of this study is the CEA elevation in post-radiotherapy samples, however, unfortunately, we could not interrogate into this phenomenon due to time constraint of the project. The elevation may be due to radiation effect and therefore more time points should have been added like 6 weeks, 8 weeks, and 12 weeks post-treatment. Usefulness of CEA as a marker in cervical patients post-radiotherapy could then be explored in a large sample size. Furthermore, the number of patients in this group was very small. In addition, we could not evaluate the significance of treatment effect of radiotherapy on the serum tumor marker levels in endometrial carcinoma patients as the sample size was too small. A large population-based study will give a better picture of the actual scenario.

CONCLUSIONS

This study has shown that, among the three tumor markers, comparison of pre- and post-treatment serum CA125 levels best reflect the treatment effects in all the three types of gynecological carcinomas. Use of CEA as a prognostic marker to observe treatment effect is not reliable alone in cervical carcinoma patients since its serum level has been found to be higher, particularly after radiotherapy, even in absence of recurrence of the disease. However, CA19.9 is reliable to evaluate treatment effect in patients of cervical and endometrial carcinomas, especially with surgery.

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Ethical approval: The study was approved by the Institutional Ethics Committee of Institute of Post-Graduate Medical Education and Research, Kolkata, India.

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