International Journal of Medical Research Professionals
P-ISSN: 2454-6356; E-ISSN: 2454-6364
DOI: 10.21276/ijmrp

IJMRP

Original Research Article

Tumor Markers Application for Diagnosis, Monitoring of Recurrence and Prognosis in Esophageal Cancer Patients Treated with Chemotherapy

Suvimal Dutta[1], Reena Banarjee[2], Karan Singh Chandrakar[2*]

[1]Assistant Professor, Department of Surgery, [2]Assistant Professor, Department of Pathology, Chandulal Chandrakar Memorial Medical College, Kurud Road, Kachandur, Durg, Chattisgarh, India.

ABSTRACT

Purpose: Tumor Markers Application for Diagnosis, Monitoring of Recurrence and Prognosis in Esophageal Cancer Patients Treated with Chemotherapy.

Methods: For the study comprising total 120 cases suffering from esophagus cancer stage I, stage II stage III and Stage IV (before and after different cycle of chemotherapy) were selected. All patients were clinically and histologically diagnosed. A total of 42 age and sex matched healthy subjects taken as control. The circulating levels of GST and CEA activity were assayed in the in the serum of control group and in patients with stomach cancer.

Results: Mean GST and CEA activity in serum were significantly higher in stomach cancer patients as compared to control ($p<0.001$). After chemotherapy (stage II) the activity of GST and CEA were significantly higher than before chemotherapy (stage I). In stage III (after second cycle of chemotherapy) activity was significantly decreased than that of stage II and the activity of GST and CEA was significantly decreased in stage IV (after third cycle of chemotherapy) than stage III (after second cycle of chemotherapy).

Conclusion: GST and CEA exhibit highest sensitivity for oesophagus cancer patients.

GST measurement in plasma may be useful tumor marker in oesophagus cancer. Alterations in serum GST levels may be helpful to predict the response of chemotherapy. The measurement of GST and CEA may be useful in monitoring of response and prediction and prognosis in patients received chemotherapy. Monitoring of GST is simple, low cost and relatively sensitive screening tool for oesophagus cancer. However the exact role of these findings in clinical practice and their utility in early detection of gastrointestinal cancers still needs further research in depth.

Keywords: Cisplastin, Capecitabine, Stomach Cancer, Tumor Marker, Chemotherapy, Glutathione-S-Transferase.

***Correspondence to:**

Dr. Karan Singh Chandrakar
Assistant Professor,
Department of Pathology,
CCM Medical College, Kachandur, Durg, Chhattisgarh, India.

Article History:

Received: 18-03-2017, **Revised:** 02-04-2017, **Accepted:** 22-04-2017

Access this article online	
Website: www.ijmrp.com	Quick Response code
DOI: 10.21276/ijmrp.2017.3.3.004	

INTRODUCTION

In spite of advancement for diagnosis and treatment; cancer is big threat to our society.[1] This is second most common disease after cardiovascular disease for maximum death in the world.[2] It accounts for about 23% death in USA and 7% in India. The world's population is expected to be 7.5 billion by 2020 and approximations predict that about 15 billion new cancer cases will be diagnosed. The prevalence of cancer in India is to be around 2.5 million with about 800,000 new cases 550,000death per annum.[3]

Cancer begins when cells in a part of the body start to grow out of control. There are many kinds of cancers, but they all starts because of out of control growth of abnormal cell. Cancer cells growth is different from normal cell growth. Instead of dying cancer cells continue to grow and form new abnormal cell. In most cases the cancer cells form a tumor. Cancer cell also grow into other tissues, something that normal cells cannot do. Growing out of control and invading other tissue are what makes a cell a cancer cell.[4] The esophagus is hallow, muscular tube that connect the threat to the stomach. It lies behind the trachea and in front of the spine. Foods and liquids that are swallowed travel through the inside of the esophagus to reach in the stomach. In adults, the esophagus is usually between 10-13 inches long and is about ¾ of an inch across at its smallest point. These layers are important for understanding where cancer in the esophagus tend to start and how they can grow.[5]

I. **Mucosa:** Thin layer lines the inside of the esophagus.
II. **Submucosa:** This is a layer of connective tissue just below the mucosa, which contains blood vessels and nerves.
III. **Muscularis Prapria:** This is a thick layer of muscle under the Submucosa.
IV. **Adventitia:** This is a outer layer of esophagus which is formed by connective tissue.

Esophageal cancer exists in main two histological types with different etiologies and epidermiologies namely esophageal adenocarcinoma (EAC) and esophageal squamous cell carcinoma (ESCC). The incidence of esophageal squamous cell carcinoma shows a decreasing trend but esophageal adenocarcinoma is increasing and overall incidence rate of esophageal cancer increasing.[6]

Based on clinical observations, excessive use of alcohol and tobacco, low socioeconomic status, poor oral health and consumption of hot drinks have been listed as risk factor for esophageal cancer. The presence of N-nitrosamine in food stuffs, low intake of fresh fruits and vegetables, vitamin and trace mineral deficiency, smoking opium, chewing betel squid, drinking mate and disease affecting the esophagus like achalasia and Plummer Vinson syndrome have been linked to esophageal squamous cell carcinoma.[7]

Certain substances in the diet may increase esophageal cancer risk for e.g. there have been suggestions as yet net well proven, that a diet high in processed meat may increase the cancer of developing esophageal cancer. Drinking very hot liquids frequently may increase the risk for esophageal cancer. This might be the result of long term damage the liquids do to the cell lining the esophagus. Overeating which leads to obesity, increase the risk of esophagus cancer.

On the other hand, a diet high in fruit and vegetables is linked to a lower risk of esophageal cancer. The exact reason for this are not clear but fruits and vegetables have a number of vitamins and minerals that may help prevent cancer.[8]

Esophageal cancer is one of the most aggressive neoplasms. One characteristics of esophageal cancer is its diversity, with high indices in Asian countries and a milder incidence in European and American countries.[9,10] Chine is one of the high incidence areas for esophageal cancer, which have highest incidence rate in the world. In India incidence rate of esophageal cancer in male is 7.6 and 5.1 in female.[11]

Most of the treatments outcomes of patients have been poor because the disease has already progressed to an advanced stage by the time it is diagnosed. Consequently, various tumor markers have been used to detect cancer at an early stage and monitor cancers. Recently many researchers and clinical practices indicate that there are some tumors markers including Carcinoembryonic antigen (CEA) and Glutathione-s-transferase (GST) are commonly found in digestive tract or gastrointestinal tract. Moreover they can be used for the monitoring of tumor recurrence and used as prognostic factor.[12-14]

Individualized chemotherapy administrated taking into account biomarkers expression may improve the response to chemotherapy and clinical outcome of patients. Therefore better understanding of the role of pharmacogenetics could help establishing an individualized chemotherapy and patients may benefit more from chemotherapy to prolong their life, as the gene which influences the clinical response to chemotherapeutics, control drug absorption, distribution, metabolism and excretion.

Glutathione-s-transferase (GSTs) are a family of cytosolic enzymes, and they play an important role in the detoxification of various exogenous and endogenous reactive species.[15] They participate in anti-oxidant defense through several mechanisms including reactive oxygen species.[16] GSTs catalyze the binding of large variety of electrophiles to the sulfhydryl group of glutathione (GSH) yielding less harmful and more water soluble molecules which can excrete via urine or bile. Since most reactive, ultimate carcinogenic forms of chemicals are generally electrophiles GST takes considerable importance as a mechanism for carcinogen detoxification.[17] GSTs distributed in liver, lung, skin, brain, esophagus, intestine, stomach, and placenta.

GSTs have attracted interest in the field of diagnosis, monitoring of recurrence and prognosis of malignancies. In most of the tumors GSTs expression in response to tumor formation is probably a resistance mechanism by which cell can survive and the source of plasma enzyme is mainly transformed cell with expression of GSTs.[18]

N.R. Hazari (2012, 2015) showed GSTs level in patients with esophagus cancer and gastrointestinal cancer respectively.[14,19] Yashiro niitsu (1989) studied GSTs as a tumor marker for gastrointestinal malignancies.[20] Palanisamy Pasupathi (2009) showed glutathione, glutathione dependent enzyme in gastric cancer patients.[21]

Carcinoembryonic antigen (CEA) is a glycoprotein. It was first identified in 1965 by Gold and Freedman in human colon cancer tissue extracts.[22] CEA currently classified under the immunoglobulin super family and functions as an intracellular adhesion molecule. In the recent years CEA has been widely used as a tumor marker in the diagnosis and monitoring of some malignancies.[23] Science the 1990s tumor marker including CEA and other have been widely used to monitor oesophagus cancer progression and even to assess the prognosis of oesophagus cancer patients although their specificities have not been satisfactory.[24-26] Therefore, the serum CEA level may be a pertinent index of tumor progression for patients with oesophagus cancer.

In trial of chemotherapy for patients with an oesophagus cancer and who had undergone a noncurative resection, we determined serum CEA levels before and after different cycles of cisplastin based chemotherapy in oesophagus cancer patients. Measurement of CEA in esophageal cancer patients poses a continuing challenge to surgeon. Major predicators of survival are the stage of the tumor at the time of presentation and the extent of the surgical restriction performed.[27] Little emphasis has been given to the value of detection of recurrent disease which has been reliant a crude method such as development of dysphasia or systemic metastases both of which herald the patients' rapid decline.

The tumor marker CEA is often elevated in patients with tumor of the gastrointestinal tract.[28] Elevated CEA levels have been used as a marker for recurrent colorectal cancer and prognostic marker for second surgery.[29] CEA has been reported to be beneficial in determining the relapse and the follow up of the response to the chemotherapy or treatment of the patients with gastric and esophageal cancer.[30]

This shows that change in tumor marker enzyme level of GSTs and CEA have role in cancer progression. Also, many clinicians try to predict the effect of chemotherapy by obtaining serial level of tumor markers during chemotherapy. In general a rising tumor marker level means tumor progression in patients who are receiving chemotherapy. In this our study, serum GST and CEA activity has been measured before and after I, II, III, IV cycle of chemotherapy in patients suffering from esophageal carcinoma compared with control group.

MATERIAL AND METHODS

Selection of Patients

For the study total 30 cases of carcinoma of esophageal stage I, Stage II, Stage III and stage IV were selected. All patients were clinically and histologically diagnosed. All patients with stage-II, stage-III and stage-IV received chemotherapy including cisplastin, 5-FU capecitabine, cyclophosphamide, Transtuzumab and doxorubicin. There are 13 males & 17 female of stomach cancer. For control total 42 normal healthy age and sex matched persons were selected. Subjects with stomach cancer and those without any evidence of any type of cancer participated in this study as listed in table.

Collection of Samples

Overnight fasting 5ml blood sample were collected before and after different cycle of chemotherapy in plain bulb. Serum was separated and used to estimation of glutathione-s-transferase, and Carcinoembryonic antigen. Serum GSTs activity measured by, using 1-chloro-2, 4 dinitrobenzene (purchased from Sigma company) as substrate, was measured according to the procedure described by Habig et al[16] and Estimation of serum CEA was carried out by using commercial available kits from accu-bind. On ELISA micro plate Immunoenzymometric assay.[28]

Treatment

According to the protocol, 63.82% (30 patients out of 47) of the patients completed three cycle of chemotherapy included the cisplastin, 5-FU. All the chemotherapy regimens were used under standard protocol. The combination of cisplastin (60-100 mg/m^2) and 5-FU (750-1000 mg/m^2) given by continuous infusion for 4-5 days after second stage.

Follow Up

Overall 47 patients were followed up at time of admitted in hospital and after discharge from hospital. Out of 10 patients follow up were lost during the follow up period. The follow up system consisted of measurement of tumor marker GST and CEA level before and after I, II, III, IV chemotherapy contineuously 3 months intervals for first 3 month and at 6 month intervals thereafter. The follow up program included, clinical examination, hematological analysis, tumor marker and enzyme assay at each checkup. Criteria for the establishment of recurrent disease included histological conformation or disease evident radiological with subsequent clinical progression and supportive biochemical data. The follow up end date was 17th December 2015. All survival patients followed up for at least 27 months. Seven patients expired during the follow up period.

Data were expressed as mean ±SD. Mean values were assessed for significance by unpaired student –t test. A statistical analysis was performed using the Statistical Package for the Social Science program (SPSS, 21.0). Frequencies and percentages were used for the categorical measures. Probability values $p < 0.0001$ were considered statistically significant.

Table 1: Distribution for control and patients

	Number of subjects (male/female)	Age-range (years)
Control	42(25/17)	25-55
Oesophagus cancer patients	120 (52/68)	25-60
Stage I	30(15/13)	25-60
Stage II	30(15/13)	25-60
Stage III	30(15/13)	25-63
Stage IV	30(15/13)	25-70

Table 2: Comparison of serum GST and CEA activity in control with oesophagus cancer

Tumor Markers	No. Of cases	Mean ± SD	" P" Value
GST IU/L	30	9.39 ± 0.61	<0.001
GST Control	42	5.05 ± 0.51	-
CEA ng/ml	30	7.33 ± 1.12	<0.001
CEA Control	42	1.55 ± 0.30	-

RESULTS

As shown in table 2 mean serum GSTs activity (mean±SD) in control using CDNB as substrate was 5.05±0.51 IU/L. Serum GSTs activity of oesophagus cancerous patients was 9.39 ± 0.61IU/L. GSTs activity was significantly higher in oesophagus cancer patients than control ($p<0.001$).

CEA activity (mean±SD) in control using commercial kits from accu-bind on ELISA micro plate Immunoenzymometric assay was 1.55±0.30. Serum CEA activity of stomach cancer patients was 7.33 ± 1.12. CEA activity was significantly higher in stomach cancer patients than control ($p<0.001$).

DISCUSSION

The present study was carried out in the Department of Biochemistry in collaboration with Dept. of Medicine and Surgery Chandulal Chandrakar Memorial Medical College and Hospital Kachandur, Durg.

Serum sample obtained from 47 esophagus cancer patients admitted for evaluation & treatment were analyzed for the assay of Glutathione-s-transferase (GST), Carcinoembryonic antigen (CEA), and routine investigation. Latter on these patients were referred for treatment to specialized BSR Apollo cancer Institute Bhilai.

Cancer is a group of disease that can cause some sign or symptoms. The sign and symptoms depends upon cancer type or where the location of cancer. Cancer has metastasized symptoms or signs of cancer appear in different part of body. After metastasis or after growth of cancer it pushes to near organs, blood vessels and nerves. It causes some signs and symptoms of cancer, but in critical area of body such as in brain, the smallest tumor can causes symptoms of cancer.

It is important to known that the some symptoms of cancer are thickening of body, nagging cough, changes in bowel movement, change in bladder habits, bleeding, stomach upset, fever, fatigue, weight loss, pain, skin changes, white spot on tongue, sores that do not heal and Indigestion but single sign or symptom is not enough to find out.

Cancer is the second most common cause of death in developed countries followed by cardiovascular disease.

Knowledge of diagnostic and prognostic factors are essential for the management of individual patients and these factors should be taken into account in the design of randomized trials and in interpreting the result of such trials.

Serum tumor markers have been used in aiding the diagnosis of gastrointestinal cancers for a long time. Previous studies reported that the elevated serum values reflect the increased secretion of tumor antigens by tumor itself.[31] However mild elevation of serum tumor marker levels in number of early-stages of cancer has been always difficult to justify as many benign pathologies may frequently cause such changes. The clinical use of tumor markers is much more beneficial in determination of prognosis assessing response to treatment and detection of early recurrence.[32,33]

The present study demonstrates that elevated level of GST, LDH, ALP and CEA occur in stomach cancer patients as composed to those obtained from normal healthy control group (Table 2). Similar findings reported by G.S. Mahammadzadeh et. Al.[34] Table 3 shows that the level of GST in stage II after first cycle of chemotherapy was significantly increased than stage I (Before chemotherapy) similar findings reported by N. R. Hazari[32] and Ranjit S. Ambad.[33] But CEA level in stage II after first cycle was significantly decreased than stage I (before chemotherapy). But after 3 weeks after second cycle of chemotherapy means in stage III level of GST and CEA significantly decreased ($p<0.001$)found in present study than stage II (after first cycle). This result indicates that patients were responded to the treatment and may in the direction of recovery. Similarly in stage IV after third cycle of chemotherapy the activity of GST and GST significantly decreased ($p<0.001$) than stage III (after second cycle), and activity become in normal range. This shows that patients were responding and totally recovered by cisplastin, 5-FU based treatment.

Table 3: Serum GST (IU/L) levels before and after I, II, III, IV comprised with control counterpart.

	No. Of Cases	Mean ±SD	p-value
Control	42	5.05 ± 0.51	-
Before Chemotherapy (Stage I)	30	9.45 ± 1.12	< 0.001*
First Cycle of Chemotherapy (Stage II)	30	13.06 ± 0.95	< 0.001**
Second Cycle of Chemotherapy (Stage III)	30	9.01 ± 0.58	< 0.001$
Third Cycle of Chemotherapy (Stage IV)	30	6.06 ± 0.42	< 0.001$$

(Values are expressed in IU/L) * Control vs Stage-I, **Stage-I vs Stage-II, $ Stage II vs Stage III and $$ Stage III vs Stage IV.

Table 4: Serum CEA (ng/ml) levels before and after I, II, III, IV comprised with control counterpart.

	No. Of Cases	Mean ±SD	p-value
Control	42	5.05 ± 0.51	-
Before Chemotherapy (Stage I)	30	17.33 ± 2.41	< 0.001*
First Cycle of Chemotherapy (Stage II)	30	8.01 ± 2.60	< 0.001**
Second Cycle of Chemotherapy (Stage III)	30	2.57 ±0.23	< 0.001$
Third Cycle of Chemotherapy (Stage IV)	30	1.44 ± 0.43	< 0.001$$

(Values are expressed in IU/L) * Control vs Stage-I, **Stage-I vs Stage-II, $ Stage II vs Stage III and $$ Stage III vs Stage IV.

Studies reported progressive increase of GSTs with advancing cancer and has been associated with poor prognosis and development of drug resistance. K. Johansson et al[35] reported GSTs protect the cells from lipid peroxidation and H_2O_2 which is increased by cisplastin based chemotherapeutic drug. Our results showed at association of serum GST and chemotherapy in oesophagus cancer. Charushila Y. Kadam, Subodhini A. Abhang[36] observed that serum GST level was significantly higher in post-operative stage II in breast cancer patients before chemotherapy as compared to healthy controls. After 3 weeks of receiving 1st adjuvant chemotherapy cycle, GST and CEA level was significant decreased as compared to levels before chemotherapy in these patients. Increased activity of serum GST in oesophagus cancer is probably a resistance mechanism by which cell can survive and source of plasma enzyme is mainly transformed to cell with over expression of GST and CEA. Similar findings reported by Ranjit S. Ambad et. al.[33]

Carcinoembryonic antigen (CEA) is used predicting & in monitoring patients with advanced cancer. Tumor markers alone cannot be used to asses response, but could be used to confirm complete response – serum tumor markers have been used in aiding the diagnosis of gastrointestinal cancers for a long time. Previous studies reported that the elevated serum values reflect the increased secretion of tumor antigen of tumor itself. However mild elevation of serum tumor markers level in a number of early stage cancers has always been difficult to justify as many benign

pathologies may frequently cause such changes. The clinical use of tumor markers is much more beneficial in determination of prognosis is assessing response to treatment & detection of early recurrences.[37]

In the study various tumor markers such as CEA has been investigated in the serum of gastric adenocarcinomas to markers. Llyas Tuncer show the serum CEA level was found to be higher in 70% cases in both cases.[38] CEA is one of the most reliable tumor associated markers used for the detection of malignancy serum CEA level are used for cancer detection determination of cancer stage recurrence & evolution of cancer therapy, especially in patients with colorectal cancer. Gion et al.[39], reported that CEA was positive in 27% of the patients with oespohagas cancer. In the same study it has been reported that the positivity rate of CEA was correlated with the stage of the disease.

In present study the activity of serum GST in stage II after first cycle of chemotherapy was significantly higher than stage I (before chemotherapy) and control but after second and third cycle of chemotherapy activity of serum GST and CEA was significantly decreased. "Thus present study suggests that elevated levels of CEA during initial diagnosis provide diagnostic and prognostic significance and it is benefited for clinical practice. CEA play an important role in diagnosis and progression of treatment procedure. The levels of CEA facilitate for management of gastrointestinal cancer patients for postoperative treatment. Postoperative increased level of CEA predicts the recurrence of disease.

CONCLUSION

The present study was conducted to assess the clinical utility of enzymes GST and CEA in oesophagus cancer. Elevation of serum GST activity is probably a resistance mechanism by which cells can survive and source of circulatory levels of enzyme is mainly transformed cell with over expression of GST. Depletion of GST level after administration of chemotherapeutic drug due to higher oxidative stress after chemotherapy. Increased levels of CEA during initial diagnosis provide diagnostic and prognostic significance and it is benefited for clinical practice. The CEA play an important role in diagnosis and success of treatment procedure. Its levels facilitate the management of gastrointestinal cancer patients for postoperative treatment. Postoperative increased level of CEA predicts the recurrence of disease.

On the basis of present study results conclude that GST and CEA exhibit highest sensitivity for oesophagus cancer patients. GST measurement in plasma may be useful tumor marker in oesophagus cancer. Alterations in serum GST levels may be helpful to predict the response of chemotherapy.

The measurement of GST and CEA may be useful in monitoring of response and prediction and prognosis in patients received chemotherapy. Monitoring of GST is simple, low cost and relatively sensitive screening tool for oesophagus cancer.

However the exact role of these findings in clinical practice and their utility in early detection of gastrointestinal cancers still needs further research in depth.

REFERENCES

1. Kotnis A, Sarin R, Mulherkar R. Genotype, phenotype and cancer. Role of low penetrance genes and environment in tumor susceptibility. J. Biosci; 2005: 30: 93-102.

2. Jemal A. Siegel R. Ward E, Murray T. Xu J, Thun MJ. Cancer stastics, 2007. CA cancer J clin 2007; 57: 43-66.

3. Nandkumar A. Consolidated report of the population based cancer registries. National cancer registry programme. Indian council of medical Research. New Delhi, India. 1990.96.

4. American cancer Society. Cancer facts and figures 2015. Atlanta Ga: American cancer Society, 2015.

5. American Joint committee on cancer. AJCC cancer staging manual: 7th ed. New York NY: Springer 2010: 103-111.

6. Ferlay J, Shin HR, Bray F, Forman D, Mathers C and Parkin DM. Estimation of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J cancer 127 (12): 2893-2917.

7. Stoner GD and Gupta A. Etiology and chemoprevention of esophageal squamous cell carcinoma. Carcinogenesis 2001; 22(11): 1737-46.

8. Kushi LH, Doyle C, McCullogh M et. al. American cancer society Guidelines on nutrition and physical activity for cancer prevention: Reducing the risk of cancer with healthy food choices and physical activity. CA Cancer J Clin 2012; 62: 30-67.

9. Zheng S, Vutton L, Sheyhidin I, et al. Northwest China. A place to learn more on oesophageal cancer Part one: behavioral and environmental risk factors. Eur J Gastroenterol Hepatol 2010; 522: 917-25.

10. Lin Y, Tostsuka Y, He Y. Epidermiology of esophageal cancer in Japan and China. J Epidemiol 2013; 23: 233-42.

11. Gajalakshmi V, Swaminathan R, Shanta V. An Independent survey to assess completeness of registration: Population based cancer. Chennai India. Asian Pac J cancer Prev 2001; 2: 179-83.

12. Molina R, Auge JM, Filella X, et al. Pro-gastrin-releasing peptide in patients with benign and malignant disease: comparison with CEA, SCC, CYFRA 21-1 and NSE in patients with lung cancer. Anticancer Res, 2005; 25: 1773-8.

13. Chen SW, Liang JA, Hung YC, et al. Clinical implications of elevated pretreatment Carcinoembryonic antigen in patients with advanced squamous cell carcinoma of the uterine cervix. Tumour Biol, 2008; 29: 255-61.

14. Post-graduation Dissertation work, submitted in Maharashtra University of Health Sciences in 2009.

15. Ketterer B. Glutathione-s-transferase and prevention of cellular free radical damage free Radic. Res. 1998; 28(6): 647-58.

16. Habig WH, Pabst MJ, and Jacoby WB. Glutathione-s-transferase the first enzymatic step in mercapturic acid formation J bio. Chem. 1974; 249: 7130-7139.

17. Aceto A, Dillio C, Angelucci S, Tenaglia R. Zezza A, Cacccuri AM, and Federici G. Glutathione elated enzyme activity in testis of patients with malignant disease. Clin. Chim. Acta 1989;183:83-86.

18. Hamid N, Shahokh MG et al. Glutathione-s-transferase activity in patients with colorectal cancer. Clin Bioac. 2005; 38: 621-624.

19. N.R.Hazari, RS Ambad, AP Thorat. Serum Glutathione-s-transferase activity in esophagus cancer patients receiving chemotherapy. BCAIJ, 2012; 6(6): 177-179.

20. Yashiro Niitsu, Yasuo Takattashi, Tadanari Saito, Yasu Ji Hirato, Nobuko Arisato, Hiroshi Maruyama, Yutaka Kohgo and Jrving listowasky. Serum Glutathione-s-transferase π as a tumor marker for gastrointestinal malignancies. Cancer 1989; 63:317-23.

21. Palanisamy Pasupathi, Ganesan Saravanan, Palanisamy Chinnaswamy, Govindaswamy Bakthavath salam: Glutathione, Glutathione dependent enzyme and antioxidant status in gastric carcinoma patients. J Appl. Biomed. 2009; 7: 101-109.

22. Staab HJ, Anderer FA, Brummendorf T, Hornung A, Fisher R. Prognostic value of preoperative serum CEA level compared to clinical staging: II stomach cancer Br J. cancer 1982; 45: 718-727.
23. Ren JQ, Liv JW, Chen ZT, Liu SJ, Huang SJ, Huang A, Hong JS. Prognostic value of the lymph node ratio in stage II colorectal cancer. Chin J cancer 2012; 31: 241-247.
24. Ohkura H. Tumor markers in monitoring response to chemotherapy for patients with gastric cancer. Jpn J clin oncol 1999; 29: 525-526.
25. Yamao T, Kai S, Kazami A, Koizumi K, Handa T, Takemoto N, Maruyama M. tumor marker CEA, CA19-9, and CA125 in monitoring of response to systemic chemotherapy in patients with advanced gastric cancer. Jpn J clin oncol 1999; 29: 550-555.
26. Takahashi Y, Takeuchi T, Sakamoto J, Touge T, Mai M, Ohkura H, Kodaria S, Okajima K, Nakazato H. The usefulness of CEA and CA19-9 in monitoring for recurrence in gastric cancer patients: a prospective clinical study. Gastric cancer 2003;6:142-5.
27. Demeester TR, Zaninotto G, Johansson KK. Selective Therapeutic approach to cancer of the lower esophagus and cardia. J Thorac cardiovasc. Surg 1988; 95: 42-54.
28. Gold P, Freedom SO. Demonstration of tumor specific antigen in human colonic carcinoma by immunological tolerance absorption techniques. J Exp Med. 1965; 121: 439-462.
29. Wanebo HJ, Rao B, Pinsky CM. et al. Preparative CEA level as a prognostic indicator in colorectal cancer NEJM. 1978; 299: 448-451.
30. Ial chenko NA, Lagutin VD, Lavik MN, Musin II. The clinica information value of an immunoenzyme study of the tumor markers CA 19-9, CEA and AFP in cancer of the stomach pancreas, colon and rectum. Vopr Onkol 1991; 37: 921-4.
31. Pasane PA, Eskelinen M, Partanen K, Pikkarainen P, Pentilla I, Alhavo E. clinical value of serum tumor marker CEA, CA50, and CA242 in distinction between malignant versus benign disease causing jaundice and cholestasis, results from a prospective study. Anticancer Res 1992; 12: 1689-94.
32. N.R. Hazari, V.S.Hatalkar. Study of glutathione-s-transferase in gastrointestinal cancer. Int. J of recent trends and technology; August 2015; 16(1): 10-12.
33. Ranjit Ambad, Suryakant Nagtilak. Measurement of activity of serum enzyme Glutathione-s-transferase as tumor marker in stomach cancer. Int. J. Med. Res. Prof. 2015, 1(3), 32-34.
34. G.S.Mohammadzadeh, S.N.Moghadam;Measurement of GST &its class-ð in plasma & tissue biopsies obtained after laparoscopy &endoscopy from subjects with oesophagus &gastric cancer. Clinical Biochemistry 2003, 36, 283-288.
35. K.Johansson, K.Ahlen; Microsomal GST-1 in anticancer drug resistance. Carcinogenesis 2007, 28(2), 465-470.
36. Charushila Y. Kadam, Subodhini A. Abhang. Evaluation of serum levels of reduced glutathione, glutathione-s-transferase and nitric oxide in breast cancer patients undergoing adjuvant chemotherapy. Int. J. Cur Res Rev, July 2013/ vol 05 [13].
37. Carcinoembryonic Antigens of the Human Digestive System. J Exp Med 1968; 183:387.
38. IlyasTuncer, HalukDulger, Ismail Uygan, Mustafa, Cetin, Ramazan, eastern Journal of Medicine 2004:72- 78,9.
39. Gion M Tremolada C, Mione R, della Palma P, Dittadi R, Zari C, Nosadini A et al Tumor markers in serum of patients with primary squamous cell carcinoma of the esophagus tumor: 489-93,751989.

Source of Support: Nil. **Conflict of Interest:** None Declared.

Cite this article as: Suvimal Dutta, Reena Banarjee, Karan Singh Chandrakar. Tumor Markers Application for Diagnosis, Monitoring of Recurrence and Prognosis in Esophageal Cancer Patients Treated with Chemotherapy. Int J Med Res Prof. 2017; 3(3):12-17. DOI:10.21276/ijmrp.2017.3.3.004