Research Article

Study of Glutathione S-Transferase in gastrointestinal cancer

N R Hazari[1], V S Hatolkar[2*]

[1]Associate Professor, Department of Biochemistry, Government Medical College, Aurangabad, Maharashtra, INDIA.
[2]Professor, Department of Biochemistry, M.G.M. Medical College, Aurangabad, Maharashtra, INDIA.
Email: nhazari60@gmail.com, veenashatolkar@gmail.com

Abstract

Glutathione S-Transferase(GST) distributed widely in tissues such as liver, lung, skin, brain, intestine and placenta. Levels of enzyme detection in serum are useful for diagnosis and prognosis of human disease. Recently GST may be useful in monitoring pathogenesis of liver disease. In the present study of serum GST was significantly higher in patients with esophagus and stomach cancer as compared to those obtained from normal healthy group. Our results showed a significant increased activity of GST in stage III patients than stage II patients of both cancers; which may trigger the progression of cancer.

Key Word: Glutathione S-Transferase(GST).

[*]**Address for Correspondence:**
Dr. V S Hatolkar, Professor, Department of Biochemistry, M.G.M. Medical College, Aurangabad, Maharashtra, INDIA.
Email: veenashatolkar@gmail.com

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INTRODUCTION

GSTs are a family of enzymes involved in detoxification of foreign compounds. They participate in anti-oxidant defenses through several mechanisms including reactive oxygen species.[1] Human cytosolic GSTs are a family of dimeric enzymes divided into the main classes α, π, μ and θ.[2] GSTs catalyze the binding of a large variety of electrophiles to the sulfhydryl group of glutathione (GSH) yielding less harmful and more water soluble molecules which can be, excreted 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.[3] Glutathione S-Transferase distributed widely in tissues such as liver, lung, skin, brain, intestine and placenta. GST in man comprises atleast four gene families μ, π, γ and microsomal glutathione-s-transferase. Levels of enzyme detection in serum are useful for diagnosis and prognosis of human disease. Recently GST may be useful in monitoring pathogenesis of liver disease has been reported by several investigators.[4, 5, 6] Recently GSTs have attracted interest in the field of diagnosis and monitoring of malignancy. The human GSTs were found to be over expressed. In most, the tumors GSTs expression in response to tumor formation is probably a resistance mechanism by which cells can survive and the source of plasma enzyme is mainly transformed cell with expression of GSTs.[7] Boccia. S. *et al.* 2006.[8] studied GSts T1 status and gastric cancer risk studies. Krishnanda. P 2007[9] conducted a study in serum GST levels in patients with oral cancers. This shows that alteration in serum total GST levels may have a role in cancer progression.

MATERIALS AND METHODS

For the study, total 92 gastrointestinal cancer patients were selected, out of which 50 cases of carcinoma of esophagus and 42 of carcinoma of stomach patients of II and III stages selected. The patients were clinically and histologically diagnosed. All patients of stage III received chemotherapy including cisplastin, cyclophosphamide and doxorubicin.

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Collection of sample

10 ml of blood was collected in a dry, clean, plan bulb form patients. After clotting the blood it was centrifuged at 3000 rpm for 10 minutes.

Control group

For the control, total 40 normal healthy persons, age and sex matched for the study group were selected.

Glutathione – S – Transferase (1) Estimation

It was done by Habig *et al.* using chemicals of reagents purchased from Sigma Chemical Company. All other reagents used were of reagent grade .

Enzyme activity was monitored by measuring the conjugation of 1-chloro, 2, 4-dinitrobenze with glutathione (10).

Procedure.

GST was estimated in 1.0 ml of incubating mixture containing 850 µl of 0.1 m phosphate buffer pH 6.5, CDNB (20 mm) 50µl reduced glutathione and 50µl of serum was added.

Reaction was followed at 1min. interval for 5 minutes by measuring absorbance 340 nm on spectrophotometer or semiautoanalyzer. Simultaneously blank was run.

Calculation

GST was estimated by using molar extinction coefficient (9.6mm-1 cm-1) of GST in IU/litre.

RESULTS

Table 1: Demographic data of gastrointestinal cancer patients

	Oseophagus	Stomach
Age (yrs) 40 – 80	61.38 ± 10.20	58.38 ± 12.29
No. of cases:-	50	42
Male	24	28
Female	26	14
Stages: - II	25	21
III	25	21

In this study, 40 control cases and 92 patients of gastrointestinal cancer were estimated.

Table 2: Serum activity of glutathione – s–transferase (IU/L) in gastrointestinal patients

	No. of Cases	Mean ± S.D	No. of Cases (values > normal)	'P' value
Control	40	5.36±0.59		
Esophagus Cancer	50	11.80±2.40	50 (100%)	<0.001
Stomach Cancer	42	10.30±2.35	39 (93%)	<0.001

Values are expressed in IU/L.

Values are given as mean ± SD.

Table 2 shows serum GST activity was statistically significant higher in patient with esophagus cancer and 39 of 42 stomach cancer had elevated value of serum GST.

Table 3: Serum GST activity in various stages of stomach cancer patients and esophagus cancer patients

	GST (IU/L)	GST (IU/L) Stomach Cancer	GST (IU/L) Oesophagus Cancer
Control (n=40)	5.36±0.59	--	--
Stage II (n=21)	--	8.43±1.95	10.03±1.13
Stage III (n=21)	--	12.02±1.09	13.56±0.85

Values are given as mean ± S.D. Control Vs Stage III – P < 0.001

Stage II Vs Stage III – P<0.001

Statistically significantly increase of serum GST activity in stage II and stage III of stomach cancer and esophagus cancer compared to control group was observed. The patients of stage III had significantly elevated than stage II.

DISCUSSION

In the present study of serum GST was significantly higher (<0.001) in patients with esophagus and stomach cancer as compared to those obtained from normal healthy control group. G. S. Muhammadzadeh *et al.*[11] observed similar result in which plasma activity was significantly higher in esophagus and gastric cancer patients. The GST activity in plasma represents a non-invasive biomarker of the cellular protection. The activity of the GST was higher in 100% patients of esophagus cancer and 93% patients of stomach cancer in this study supports the finding of Niitsu *et al.*[12] and Tsucida *et al.*[13] The increased activity of GST π class was found to be over expressed in most of tumor.[14] Our results showed a significant increased activity of GST in stage III patients than stage II patients of both cancers; which may trigger the progression of cancer. GST II expression in malignant tissue and plasma GST II levels in human colorectal and gastric cancer are believed to increase depending on the stages of tumor.[13] Many studies also showed progressive increased of GST with advancing cancer and has been associated with poor prognosis and development of drug resistance.[15,16] Elevation of serum GST activity in esophagus and stomach cancer is probably a resistance mechanism by which cells can survive and source of plasma enzyme is mainly transformed to cell with over expression of GST. In the present study the serum GST level in stage III (received chemotherapy) of both cancers was significantly elevated than stage II and control group and suggests that enhanced antioxidant made the tumor tissue less susceptible to oxidative stress conferring growth advantage. K.Johnson *et al.*[17] reported GST protects the cells from lipid peroxidation and from hydrogen peroxide. Our findings suggests that elevation

of serum GST activity is probably a resistance mechanism by which cells can survive and source of plasma enzyme is mainly transferred cell with over expression of GST. On the basic of our result we conclude that GST measurement in plasma may be useful as tumor marker in gastrointestinal caner. Alterations in serum GST level might be helpful to predict the response of chemotherapy.

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