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

IJMRP

Original Research Article

Measurement of Activity of Glutathione Peroxidase (Gpx) and Superoxide Dismutase (SOD) in Upper Gastrointestinal Cancer Patients

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ABSTRACT

Purpose: Measurement of activity of Glutathione peroxidase (Gpx) and Superoxide dismutase (SOD) in Upper Gastrointestinal Cancer Patients.

Methods: For the study comprising total 30 cases suffering from esophagus cancer and 30 cases suffering from stomach cancer were selected. All patients were clinically and histologically diagnosed. A total of 50 age and sex matched healthy subjects taken as control. The circulating levels of SOD and GPx activity were assayed in the in the serum of control group and in patients with Upper GIT cancer.

Results: Mean SOD and Gpx activity in serum were significantly decreased in upper GIT cancer patients as compared to control ($p<0.001$).

Conclusion: In the present study I concluded that the activity of SOD and Gpx were significantly decreased found in upper gastrointestinal cancer patients because reactive oxygen species (ROS) are generated through numerous normal metabolic processes and are needed for normal functioning of the organism. Various antioxidant enzymes like superoxide dismutase (SOD) and glutathione peroxidase (GPx) control their accumulation. Oxidative stress caused by increased free radical generation and decreased antioxidant level in the target cells and tissues has been suggested to play an important role in carcinogenesis. In this study antioxidant enzyme SOD with and Gpx shows positive correlation.

Keywords: Stomach Cancer, Esophagus Cancer, Antioxidant, Reactive Oxygen Species, Glutathione Peroxidase.

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Article History:

Received: 19-03-2017, **Revised:** 03-04-2017, **Accepted:** 23-04-2017

Access this article online	
Website: www.ijmrp.com	Quick Response code
DOI: 10.21276/ijmrp.2017.3.3.009	

INTRODUCTION

Gastrointestinal tract is one of the important organs after heart and brain. Though definitely not the most attractive organs in the body, but they are certainly among the most important. It is more than 30 feet long tube which initiate from mouth to an anus and responsible for many different body functions. The GI tract is imperative for our well-being throughout life. A nonfunctional or poorly functioning GI tract can be the source of many chronic health problems that can interfere with quality of life. The gastrointestinal system is responsible for breakdown and absorption of food and liquid needed to sustain life. Many different organs have essential role in the digestion of food. The GI tract starts with mouth and proceeds to esophagus, stomach, small intestine, large intestine, rectum and terminates at the anus.

Cancer is group of diseases characterized by uncontrolled growth and spread of abnormal cells. If the spread is not controlled, it can result in death. Cancer is caused by both external and internal factors. These factors may act together or in sequence to initiate or promote carcinogenesis. The development of most cancers requires multiple steps that occur over many years. Certain types of cancers can be prevented by eliminating exposure to tobacco and other factors that initiate or accelerates this process.

Gastric cancer is one of the leading causes of death from cancer in worldwide, with a million of new cases diagnosed each year. Indeed, it is the fourth most common cancer and the second leading cause of cancer death. The incidence of gastric cancer is different throughout the world and 60% of deaths from gastric cancer occur in developing countries.[1] Gastrointestinal (GI) cancers include cancers of the esophagus, stomach, intestines, colon, rectum, pancreas, and terminates at the anus. The asymptomatic onset and development of GI cancers advances frequently up to stage at time of diagnosis which can be more fatal during that period. The most common mode of the GI cancer deaths is due to metastasis and peritoneal carcinomatosis.[2] Malignancies of the G.I. tract are relatively resistant to radiation therapy and chemotherapy has also had modest benefit, whereas an effective therapy still remains elusive in the treatment of gastroduodenal ulceration. Early diagnosis of human gastric cancer or tumor recurrence is primarily based on endoscopy,

biopsy and pathological examination. Endoscopy is a widely used method for detecting early stage of gastric cancer.[3]

In India, the incidence of gastric cancer is very low compared to that in Western countries, and the number of new gastric cancer cases are approximately 34,000, with a male predominance, (male to female ratio is 2:1). It is estimated that by the year 2020, approximately 50,000 new cases of gastric cancer will be reported annually in India. Recent National survey of cancer mortality in India indicated that gastric carcinoma was the second most common cause of cancer related deaths amongst men and women.[4] Annual incidence rate of stomach cancer in India is 10.6 per 100,000 populations. Whereas the incidence rate in male is 5.7 per 100,000 in men and in female are 2.8 per 100,000 in women.[5] The incidence of gastric cancer has been relatively high in Southern India; however recent data indicate that the incidence rates are the highest in the north-eastern region of India.[6] As per latest reports available from National Cancer Registry Programme among the older registries, the incidence rate of gastric cancer documented as below.[7,8]

One of the common denominators for the genesis of these diseases is the involvement of free radicals. Oxidative stress caused by increased free radical and decreased antioxidant level in the target cells and tissues has been suggested to play an important role in carcinogenesis.[9] Free radicals are capable of altering all major classes of biomolecules, such as lipids, nucleic acids and proteins, with changes in their structure and function.[10] The levels of free radical molecules are controlled by various defense mechanisms, it consists of enzymatic and non-enzymatic mechanisms.

MATERIAL AND METHODS

Selection of Patients

Present study comprising total 30 cases of carcinoma of stomach and esophagus. All patients were clinically and histologically diagnosed. There are 15 males and 15 females of stomach cancer and 13 males and 17 females of esophagus cancer. For control total 50 normal healthy age and sex matched persons were selected. Subjects with stomach and esophagus cancers and those without any evidence of any type of cancer participated in this study as listed in following table.

Collection of samples

Overnight fasting venous 5ml blood samples were collected in plain bulb. Serum was separated and used to estimate glutathione peroxidase and Superoxide dismutase. Serum Gpx activity measured by, using Hafeman D G, et al. method.[11] For Estimation of Superoxide dismutase was done by using Mishra H. P., Fridovich I, et al., method.[12]

Data Analysis

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 $p < 0.001$ were considered statistically significant.

Table 1: Distribution for control and patients

	Number of subjects (male/female)	Age-range (years)
Control	50(25/17)	25-60
Stomach cancer patients	30 (15/15)	20-65
Esophagus cancer patients	30(13/17)	28-65

Table 2: Distribution of control and cancer cases according to their age.

Age wise Distribution (Yrs)	Control [n= 50]				Stomach Cancer patients (n=30)				Esophagus Cancer Patients (n=30)			
	Male	Female	Total	%	Male	Female	Total	%	Male	Female	Total	%
25-35 yrs	14	5	19	38	1	2	3	10	1	1	2	6.7
36-45 yrs	10	11	21	42	4	1	5	16.6	1	4	5	16.7
46-55 yrs	5	3	8	16	7	6	13	43.3	6	6	12	40
56-65 yrs	2	0	2	4	3	6	9	30	5	6	11	36.7
Total	31	19	50	100	15	15	30	100	13	17	30	100

OBSERVATIONS AND RESULTS

We observed age wise distribution of the control subjects in age group 25-65 yrs and patients i.e. stomach and esophagus cancer cases were listed in table 2. We observed gender distribution in study patients both stomach and esophagus cancer cases among control group as shown in table 3. Biomedical Parameter of the individuals studied in the present study is given in table 4, the basal level of SOD and Gpx in control and cancer patients suffering from Stomach and Esophagus. Table 4 Shows the SOD and Gpx activity was statistically significantly lower in patients with esophagus and stomach cancer than control group. The 30 of 30 patients of esophagus cancer and 24 of 30 patients of stomach cancer had lowered value of serum SOD. The 27 of 30 patients of esophagus cancer and 24 of 30 patients of stomach cancer had decreased value of Gpx.

Table 3: Distribution of genders in study subjects and control group

	Control (n=42)		Stomach Cancer Patients		Esophagus Cancer Patients	
Sex	**Frequency**	**%**	**Frequency**	**%**	**Frequency**	**%**
Male	31	62	15	50	13	43.33
Female	19	38	15	50	17	56.66
Total	50	100	30	100	30	100

Table 4: Biomedical Parameters of control, stomach and esophagus cancer.

Biomedical Parameters	Control (n=50) Mean ± S. D	Stomach Cancer (n=30) Mean ± S. D	Esophagus cancer (n=30) Mean ± S. D	'P' Value
SOD mg/ ml	11.09 ± 1.16	8.76±0.87	8.73±2.89	<0.001
Gpx (U/mg of Hb	7.81 ± 0.45	6.17±1.23	5.97±1.54	<0.001

DISCUSSION

The present study was carried out in the Dept. of Medicine collaboration with Dept. of Surgery at Shri Shankaracharya Institute of Medical Science, Junwani, Bhilai. Serum sample obtained from 30 stomach and 30 esophagus cancer patients admitted for evaluation & treatment were analyzed for the assay of glutathione peroxidase (Gpx) and Superoxide dismutase (SOD) and routine investigation. Latter on these patients were referred for treatment to specialized BSR Apollo cancer Institute Bhilai and cancer Hospital Raipur.

Reactive oxygen species (ROS) are superoxide radicals (O_2), hydrogen peroxide (H_2O_2), hydroxyl radicals (OH) and singlet oxygen which occur in small amounts during normal oxygen metabolism. Reactive oxygen species can initiate free radical chain reactions where various free radicals can form.[13] Activation of macrophage, neutrophils and the electron transport chain due to ultraviolet rays, metal catalyzed reactions, atmospheric pollution and inflammation are the factors that cause ROS production.[14] Increase in oxygen molecules that can happen at certain levels is deactivated by the natural antioxidant molecules which are always present in certain amounts in the body. This allows the oxidant levels and the deactivation power of antioxidants in an organism to remain in balance.[13] The delicate balance between free radicals and antioxidant defense system shifting in favor of pro-oxidant and oxidants, leads to the development of stress and plays an important role in the progress and development of various type of cancer.[15]

Oxygen is highly reactive species that has the ability to become part of potentially harmful and damaging molecules (Free Radicals). Oxidative stress causes healthy cells of the body to lose their function and structure by attacking them. Up until now, pathogenesis of about more than 50 diseases has been implicated by free radicals.

It is when the antioxidant level is limited that this damage can become debilitating and cumulative. Damage to DNA, proteins, lipid and other macromolecules due to oxidation has been implicated in the pathogenesis of a wide variety of diseases, most notably cancer disease.[16]

Free oxygen radicals are primarily removed by various enzymatic antioxidants like Superoxide dismutase (SOD), glutathione peroxidase (GPx), and non-enzymatic antioxidants like glutathione (GSH), and vitamin- C.[17] Superoxide dismutase (SOD) is an important antioxidant enzyme that protects cells from free oxygen radical toxicity. SOD catalyses the dismutation of superoxide radicals into hydrogen peroxide and molecular oxygen.[18] Glutathione peroxidase (GPx) is the enzyme responsible for reducing hydroperoxides. This is a cytosolic enzyme of tetrameric structure that contains four selenium atoms. GPx that uses glutathione as a substrate plays an important role in defense against free oxygen radicals, peroxides and carcinogens.[19]

Glutathione is a tripeptide consisting of glutamic acid, cysteine and glycine and has a high level of intracellular concentration. Glutathione, a significant reduction agent and antioxidant, sustains the oxidation reduction balance of cells and protects them from the negative effects of endogenous and exogenous source of oxidants.[20] Glutathione and relevant enzymes in cells act to deactivate endogenous and exogenous toxic components, free radicals, and reactive oxygen species, such as peroxides that cause damage to the liver and other tissues (J. D. Hayes J D, et al., 1999). A reduction in antioxidants can disrupt the balance between pro and antioxidants and cause cellular damage and resulting malignant transformation. Moreover, an oxidative environment with excessive ROS production can affect critical cellular structures, including chromosomes that regulate gene expression.[21]

Our study shows that the similar trend of antioxidant enzyme deprivation a marker of failing defense oxidative stress. A highly significantly decreased (P<0.001) levels of SOD (8.74±1.1.26) were found in cancer patients than control group (11.09 ± 1.16) and GPx activity also highly significantly decreased found in (6.07±1.17) in patients than normal healthy control subjects (7.81 ± 0.45).

We also observed that the activity of SOD was stastically highly significantly decreased in esophagus and stomach cancer patients was 8.73±2.89 and 98.76±0.87 respectively and the activity of GPx in esophagus and stomach cancer patients was 5.97±1.54 and 6.17±1.23 respectively, than normal healthy control subjects. Above result shows that the continuous decrease of antioxidant enzymes activity may be due to increase level of ROS generation. However, similar findings showed by Pasupathi P, et al.[22] (2009); Tandon R et al.[23] (2004); they show decreased level of antioxidants enzyme SOD an Gpx in diverse malignancies of esophagus and stomach cancer patients.

CONCLUSION

In the present study I was found that the activity of SOD and Gpx were significantly decreased found in upper gastrointestinal cancer patients because reactive oxygen species (ROS) are generated through numerous normal metabolic processes and are needed for normal functioning of the organism. Various antioxidant enzymes like superoxide dismutase (SOD) and glutathione peroxidase (GPx) control their accumulation. Oxidative stress caused by increased free radical generation and decreased antioxidant level in the target cells and tissues has been suggested to play an important role in carcinogenesis. In this study antioxidant enzyme SOD with and Gpx shows positive correlation.

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Source of Support: Nil.

Conflict of Interest: None Declared.

Cite this article as: Ravindra Kulkarni, Manjjari Kulkarni. Measurement of Activity of Glutathione Peroxidase (Gpx) and Superoxide Dismutase (SOD) in Upper Gastrointestinal Cancer Patients. Int J Med Res Prof. 2017; 3(3):38-41.
DOI:10.21276/ijmrp.2017.3.3.009