Summary

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. Gastrointestinal (GI) cancers include cancers of the esophagus, stomach, intestines, colon, rectum, pancreas, liver, and bile duct. This is a class of diseases in which a group of cells display uncontrolled growth, invasion and sometimes metastasis. 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 stages of gastric cancer.

One of the common denominators for the genesis of these diseases is the involvement of free radicals. 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), catalase (CAT) 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.

Pepsinogen is the inactive precursor of pepsin, two groups have been immunochemically and biochemically identified, Pepsinogen A (PG-I) and Pepsinogen-C (PG-II). Pepsinogen A (PGA) is localized mainly in the fundus and pepsinogen C (PGC) is found throughout the stomach and in the proximal duodenum. The Pepsinogen-C gene has been localized to 6p11-6p21. Taggart R T, et
al, 1991 have reported that a region of the human Pepsinogen-C gene contains some gene polymorphisms. Pepsinogen are considered as effective markers of terminal differentiation of the stomach mucosa, and also of preneoplastic and neoplastic changes in the tissue. As far as we are aware, there are few studies of pepsinogen-C gene polymorphisms and the relationships between polymorphisms and serum pepsinogen-II levels have not been investigated. This study clarifies the correlation between the pepsinogen-C gene polymorphism and serum pepsinogen-II and determination of the changes in the levels of above biochemical parameters can be considered as valuable markers in respect of diagnosis as well as in respects of favorable prognosis in gastrointestinal carcinoma.

The present study was carried out in the Department of Biochemistry and Department of Radiation Oncology, J. A. group of hospitals, G.R. Medical College, Gwalior. The study was conducted in 300 human subjects, out of which 100 age matched normal healthy controls were considered as control Group-I and 200 were Gastrointestinal Carcinoma patients (Group-II) and Group-II farther divided in three sub-Group, esophagus cancer (Group-IIA), Stomach cancer (Group-IIB) and colorectal cancer (Group-IIC). Written consent from all subjects also taken before study. The 05ml of blood sample was collected from healthy control and GI cancer patient for biochemical and molecular investigation.

The blood sample was analyzed for the following parameters:-

**Biochemical Investigation:**

**Oxidative stress marker:** Plasma Malondialdehyde (MDA).

**Endogenous Antioxidants:** Superoxide Dismutase (SOD), Glutathione Peroxidase (GPx), 
Exogenous Antioxidants: Vitamin-C.

Biochemical marker: Serum glutamate oxaloacetate transaminase (SGOT), Serum glutamate pyruvate transaminase (SGPT), Total Protein (TP).

Gastric Enzymes: - Serum Amylase, lipase and Pepsinogen-C (PGC/PG-II).

Molecular Investigation: Pepsinogen-C (PGC) gene polymorphism.

SPSS 16 was used for all statistical analyses. All parameters were given as mean ± standard deviation. Student’s t-tests (paired & unpaired), chi square test and one way ANOVA were used to compare the mean values of variables between the two groups. Correlations between variables were analyzed by Pearson’s correlation test. P-values < 0.05 were considered significant. Allele and genotyping frequency were calculated by the X² test to test deviation from the Hardy-Weinberg equilibrium (HWE).

We summarize our study as:

- In the present study, the plasma Malondialdehyde (MDA), an extent of lipid peroxidation was highly significantly (p<0.001) increased in Gastrointestinal cancer patients along with all sub-Group-IIA, IIB and IIC as compared with healthy control (Group-I). The findings clearly show that the increase of lipid peroxidation and its peroxidation product MDA is due to disease condition and poor antioxidant defense mechanism.

- Major finding of this study is the comparison of antioxidant enzymes activities of all gastrointestinal cancer group and we found highly significant decrease (p<0.001) mean level of all these antioxidant enzymes (SOD, GPx and Vit.-C).
We found that gastric enzymes serum Lipase, Amylase and Pepsinogen-C mean level were statistically increased in all study groups as compared to controls.

The correlation study between all parameters in gastrointestinal cancer patients. It was found plasma MDA had negative correlation with superoxide dismutase, Glutathione Peroxidase and Vitamin-C while significantly positive correlation with gastric enzymes lipase and Pepsinogen-C. The studied antioxidant enzyme SOD with Gpx and Vit-C shows positive correlation and gastric enzymes Pepsinogen–C with SOD, Gpx and lipase shows negative correlation.

In our study, we observed that, the mean level of gastric enzyme serum Pepsinogen-C was highly significant increased (P< 0.001) in group-II as compared with healthy control (group-I) subjects.

04 alleles (310bp, 400bp, 450bp and 480bp) of pepsinogen-C gene with different size base pair band were obtained (by PCR Machine)

In the present study, the frequency of Allele 1(310 bp) was higher in patients with gastric cancer compared to control group and was statistically significant (p<0.001). Genotypes containing homogenous allele 1(310 bp) were significantly more frequent in patients with gastric cancer than those in controls and was statistically significant (p<0.001). This result showed that there is relation between the pepsinogen C gene polymorphism and gastric cancer, and the person with homogenous allele 1 seems to predispose to gastric cancer than those with other genotypes.

Based on the observations, following conclusions can be drawn:
1. Firstly, we report here that there is an increase in MDA levels and a decrease in the levels of antioxidant enzymes (SOD & GPx) and Vit C in gastrointestinal cancer patients as compared to controls. This indicates that there was imbalance between oxidant and antioxidant system in case of gastrointestinal cancer.

2. Secondly, we found increased levels of serum gastric enzymes i.e. amylase, lipase and Pepsinogen-C in gastrointestinal cancer patients compared to controls. This indicates that serum PEPSINOGEN-C may be used as a marker for the diagnosis of gastrointestinal cancer.

3. Thirdly, the results suggest that there is some relation between pepsinogen C gene polymorphism and gastric cancer and the person with homogenous allele 1 (310 bp) predisposes to gastric cancer than those with other genotypes. Thus, Pepsinogen C gene polymorphism may be used as a genetic marker for a genetic predisposition to gastric cancer.