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BIOCHEMICAL INVESTIGATIONS IN GASTRIC CANCER PATIENTS

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ABSTRACT

Gastric cancer is one of the most common malignant diseases with one of the highest mortality rates worldwide. Over 95% of gastric cancer cases are adenocarcinomas. The study aim is to detection of Tumor Markers and other Biochemical investigations in the serum. 60 gastric cancer patients, 36 were male and 24 were female aged 43-65 years and 100 health control group, 50 males and 50 females aged 44-64 years were included in this study. Increased Total cholesterol, triglycerides, alkaline phosphatase, creatinine, uric acid, BUN (Blood Urea Nitrogen), CK-MB, LDH levels were found and decreased HDL levels were found in patients with gastric cancer when compared with healthy controls. The combined detection in the blood biochemical investigations and tumor markers is of important reference value for screening of patients with gastric cancer and can provide the basis for early

treatment of the disease. With a larger trial, we would be able to make more definitive statements regarding the importance of these biochemical parameters and the proper timing for measurement.

Keywords: Adenocarcinoma, Tumor Markers, Helicobacter pylori, Carcinoma Embryonic Antigen

INTRODUCTION

Stomach cancer is the second most common cause of cancer-related death in the world – it leads to around 800,000 deaths each year, yet it is only the fourth most commonly diagnosed cancer, with around one million people diagnosed each year [1]. Gastric cancer (GC) ranks fourth in incidence (after lung, breast and colorectal) and second in mortality (after lung cancer) among all cancers worldwide [2]. The early screening of gastric cancer is costly and opportunistic screening in outpatient service has been adopted all the way in our country, leading to early diagnosis rate lower than 10% [2].

Both genetic and environmental factors are involved in GC development³. Recent epidemiological and clinical investigations have evidenced the relationship between inflammation and development of gastrointestinal cancers [4, 5]. Helicobacter pylori infection is considered to be the leading cause of gastric mucosa inflammation [6]. Gastritis is followed by the activation of neutrophils, leukocytes, macrophages, and platelets. Long-standing inflammation promotes the

stomach wall ulceration and may initiate the cancer pathway: inflammation-metaplasia-dysplasia cancer [7, 3]. Development of GC is usually asymptomatic; therefore, it is diagnosed at the advanced stage.

Gastric cancer is a result of multiple factors and the detection of a single marker is often of the contradiction between specificity and sensitivity, so the combined detection of multiple markers is of great significance for the screening and diagnosis of gastric cancer [7]. Blood testing is a widely accepted method in this regard and that the combined detection of multiple tumor markers in serum has been widely used for cancer diagnosis [8].

Present study explored and analyzed the clinical value of combined detection in the blood biochemical investigations and tumor markers in screening of gastric cancer patients so as to provide strong support for accurate identification of gastric cancer prevalent population. So we designed the study aim is to detection of Tumor Markers and other Biochemical investigations in the serum.

MATERIAL AND METHODS

60 gastric cancer patients, 36 were male and 24 were female aged 43-65 years and 100 health control group, 50 males and 50 females aged 44-64 years were included in this study. The present study was conducted with the established and histopathologically confirmed gastric cancer. The blood samples (5 ml) each were collected from each patient aseptically in heparinized tubes. The samples were then centrifuged at 2000 rpm for 15 min. The plasma of the samples were then collected in sample vials and kept in the freezer till the samples are analyzed for the biochemical profile and Tumor Markers. The collected samples were analyzed for various biochemical parameters including blood sugar, total cholesterol, triglycerides, HDL-C, total protein, albumin, globulin, A:G ratio, bilirubin (direct & total), creatinine, BUN, uric acid, calcium, phosphorus, cholinesterase, SGOT, SGPT, alkaline phosphatase, gamma glutamyl transferase, lactate dehydrogenase, amylase etc. All the biochemical parameters were analyzed on a fully siemens automated analyzer. Carcinoma Embryonic Antigen (CEA) and CA125 done by ELISA method.

Statistical Analysis

Data analysis was conducted using SPSS, version 11.5. Descriptive statistics were presented as mean [standard deviation

(SD)] for quantitative data. Analysis of variance (ANOVA) was used to test the significance of the mean differences

RESULTS

In the present analysis of serum biochemical profile of the gastric cancer patients the Fasting blood glucose level was 106.17 ± 1.78 mg/dl. The plasma total protein and albumin levels were 7.29 ± 0.89 g/dl and 3.89 ± 0.09 g/dl respectively. The total and direct bilirubin levels observed were of 0.70 ± 0.02 mg/dl and 0.26 ± 0.18 mg/dl. The observed blood urea nitrogen (BUN) level was 16.42 ± 1.80 mg/dl. The uric acid level observed was 6.38 ± 1.81 mg/dl. The observed value for creatinine was 2.1 ± 0.79 mg/dl. Plasma calcium and phosphorus levels observed were 8.92 ± 1.29 mg/dl and 3.72 ± 0.57 mg/dl levels were found when compared with controls. The total cholesterol, triglyceride and HDL-Cholesterol levels were 241.12 ± 51.72 mg/dl, 186.65 ± 64.32 and 37.15 ± 8.54 mg/dl respectively when compared with control group. The observed levels of total cholesterol and triglyceride were higher than the normal values reported while the observed HDL Cholesterol level was lower than the normal range.

Table 1: Serum Biochemical Investigations of Gastric Cancer Patients (M±SD)

Test	Mean ± SD		Normal Ranges
	Patients	Controls	
Glucose (mg/dl)	106.17 ± 1.78	93.4 ± 28.82	70 – 110 mg/dl (Fasting)
Lipid Profile			
Total Cholesterol (mg/dl)	241.12 ± 51.72	188.63 ± 12.80	< 200 (mg/dl)
Triglycerides (mg/dl)	186.65 ± 64.32	169.67 ± 8.64	< 200 (mg/dl)
HDL –Cholesterol (mg/dl)	37.15 ± 8.54	49.59 ± 4.17	Male 37-67 (mg/dl) Female 40-71 (mg/dl)
Liver Function Tests			
Total Protein (g/dl)	7.92 ± 0.12	7.29 ± 0.89	6.0-8.0 (g/dl)
Albumin (g/dl)	4.19 ± 0.25	3.89 ± 0.09	3.5-5.0 (g/dl)
Total bilirubin (mg/dl)	0.5 ± 0.18	0.70 ± 0.02	0.2-1.0 (mg/dl)
Conjugate bilirubin (mg/dl)	0.28 ± 0.19	0.26 ± 0.18	< 0.3 (mg/dl)
AST (IU/L)	38.0 ± 2.99	34.33 ± 4.51	< 35 (IU/L)
ALT (IU/L)	30.97 ± 4.80	17.21 ± 10.61	< 40 (IU/L)
Alkaline phosphates (IU/L)	139.1 ± 20.92	102.16 ± 1.62	Children (1-14 yrs) < 90 (IU/L) Adult <146 (IU/L)
Renal Function Tests			
Urea (mg/dl)	42.3 ± 9.31	23.61 ± 5.12	10-40 (mg/dl)
Creatinine (mg/dl)	2.1 ± 0.79	0.79 ± 0.03	< 1.5 (mg/dl)
Uric Acid (mg/dl)	6.38 ± 1.81	3.5 ± 0.6	< 7.0 (mg/dl)
BUN (mg/dl)	2.42 ± 1.80	12.24 ± 1.30	10-20 (mg/dl)
Enzymes			
Amylase (IU/L)	52.23 ± 4.42	48.35 ± 4.10	< 90 (IU/L)
Lipase (IU/L)	132.32 ± 52.36	93.21 ± 38.26	< 146 (IU/L)
Iso Enzymes			
CPK – MB (IU/L)	89.32 ± 12.91	13.38 ± 1.36	< 25 (IU/L)
LDH (IU/L)	456.32 ± 39.32	139.32 ± 6.92	< 414 (IU/L)
Other Routine Biochemistry tests			
Calcium (mg/dl)	8.92 ± 1.29	8.13 ± 0.72	9-11 (mg/dl)
Phosphorus (mg/dl)	3.72 ± 0.57	3.69 ± 0.52	2.5-3.8 (mg/dl)

Table 2: Comparison of general information in 2 groups

Group	No. of Cases	Sex		Age (Yrs)	P Value
		Male	Female		
Study Group	60	36	24	54.6 ± 4.9	> 0.05
Control Group	100	50	50	54.3 ± 4.7	> 0.05

Table 3: Comparison of tumor markers between 2 groups

Group	No. of Cases	CEA (ng/ml)	CA 125 (IU/ml)	P Value
Study Group	60	27.32 ± 8.43	65.34 ± 5.03	< 0.01
Control Group	100	8.31 ± 1.56	18.9 ± 6.01	< 0.01

DISCUSSION

Increased Total cholesterol, triglycerides, alkaline phosphatase, creatinine, uric acid, BUN (Blood Urea Nitrogen), CK-MB, LDH levels were found and decreased HDL levels were found in patients with gastric cancer when compared with healthy controls. There is no statistically significant changes of Fasting

blood sugar, total protein, albumin, total bilirubin, conjugate bilirubin, AST, ALT, Urea, calcium, phosphorus, amylase, lipase levels were found when compared with healthy controls.

Increased total cholesterol, triglycerides, alkaline phosphatase, creatinine, uric acid, BUN (Blood Urea Nitrogen), CK-MB, LDH levels were found

in patients with gastric cancer when compared with healthy controls.

Increase level of serum total cholesterol and decrease in HDL-Cholesterol among the gastric cancer patients compared to the normal and controls was also reported by Monharan and his colleagues [9]. Environmental factors and lifestyle of the individuals have been implicated in the genesis of stomach cancer. Alterations in blood lipids in smokers have been reported by Craig and colleagues [10]. Pugalendi and Ramakrishnan [18] reported increased total cholesterol with concomitant decrease in HDL-Cholesterol among smokers. Alcohol is also known to cause changes in the concentration of lipoprotein cholesterol [12]. The enhanced plasma total cholesterol level in gastric cancer patients can cause an increase in plasma LDL with suppression of LDL receptor activity, resulting in a further increase in plasma cholesterol levels. The observed increase in the plasma total cholesterol and decrease in HDL-Cholesterol among the gastric cancer patients in the present investigation may be related to the lifestyle of the patients as most of the this area people are heavy smokers and also consumes the smoked meat.

CEA is of glycoprotein structure and located on the membrane of cancer

cells. There may be a trace amount of CEA in serum of the normal population, while in patients with gastric cancer, CEA will be of higher concentration because it will gradually fall off from the cell membrane and enter body fluids with the occurrence and growth of tumor cells, from which clinical researchers attempt to detect CEA in serum for diagnose of tumors like esophageal cancer, gastric cancer, colorectal cancer and other gastrointestinal tumor [13]. CA125 is the most sensitive marker in patients with epithelial ovarian cancer and has moderately high positive detection rate in gastric cancer sufferers. A large number of studies have shown [14-16] that the changes in the level of CA125 reflect the invasion of the tumor to the body. In this study, the tumor markers of CEA and CA125 were significantly increased in the study group compared with the control group ($P < 0.05$), suggesting that the levels of serum CEA and CA125 were higher in patients with gastric cancer than in healthy subjects. We also found that compared with the control group the levels of serum total cholesterol, HDL and LDL significantly decreased in the study group with the differences being statistically significant ($P < 0.05$).

Cholesterol, a main component of cell membrane [17], may be involved in the occurrence and development of gastric

cancer through direct or indirect mechanism and particularly the cholesterol demand is expected to increase in the mitosis of tumor cells which is uncontrolled by the body, thus resulting in a great reduction of cholesterol content, a decreasing trend of TC level and a significant increase trend of LDL-C and HDL-C. When clinically manifested, gastric cancer has an extremely poor prognosis since the 5-year survival rate using currently available treatments, surgery and radio-chemotherapy, is less than 20% [18]. Therefore a potential benefit could be expected if we had a feasible diagnostic test for follow-up of patients with H. pylori gastritis and were able to predict the risk of development of stomach cancer.

These biological findings imply that LDH may be relevant to tumour growth and severity, and may also play a role in carcinogenesis. Considering the link of LDH with other chronic diseases that may leads to death [19]. Increasing of LDH levels may be LDH-A, the enzyme responsible for transforming pyruvate into lactate, plays an important role in the process of glycolysis. Several research have reported that the expression of LDH-A could be induced by a number of oncogenes²⁰. These reports support the idea that LDH-A induction is critical for the

oncogenic activity of these oncogenes in cancer cells [20].

Serum CEA can be detected in patients with alternative types of carcinoma, thus, it exhibits low specificity and sensitivity. Gastric cancer is a noteworthy disease due to its heterogeneous properties. Although the molecular basis of gastric cancer has been thoroughly investigated, resulting in significant progression within the field, ubiquitous biomarkers are rare. Therefore, the identification of novel and specific markers to diagnose and predict gastric cancer survival is important. CEA is one of the most reliable tumor associated markers used for the detection of malignancy. Serum CEA levels are used for cancer detection, determination of cancer stage and recurrence, and evaluation of cancer therapy. CEA has been reported to be beneficial in determining the relapses and the follow up of the responses to the treatment of the patients with gastric and esophageal cancers. The results of previous study [13, 18, 20] indicated that serum CK-18 is not a much more sensitive marker than CEA and CA19-9 in esophageal and gastric carcinomas.

In our study CK-MB level to increase provided evidence that the elevated total CK level was due to abdominal muscle transaction. It is used in

evaluation of myocardial injury, was such a widely available indicator that could be applied for primary cancer screening in clinical laboratories. The clinical conditions that could lead to a high CK-MB-to-total-CK ratio rather than the neoplasms. Present results showed that increased uric acid level may be a protective agent. A significant rise in uric acid level in untreated women of breast cancer patients, which may be due to high oxidative stress. In the present study, uric acid level is found to be higher than the normal range similar to the other studies. In the present study, the increased ALP level was noticed during different chemotherapy courses. This indicates the metastasis of Gastric cancer either to bone or liver. Some studies didn't found any significant difference in ALP levels in non-metastatic Gastric cancer.

Results are increasing or decreasing level of biochemical components of blood and hence affecting organ system. Increased level of bilirubin alkaline phosphatase, blood urea nitrogen and uric acid directly affects the functioning of liver and kidney. The study of serum biochemical parameters may be a helpful diagnostic tool in the monitoring of disease, metastasis and different treatment strategies of gastric cancer.

CONCLUSION

The serum triglycerides, total cholesterol, alkaline phosphatase and CEA,

CA125 and CKMB levels were higher in gastric cancer patients while the HDL-Cholesterol level was lowered. The combined detection in the blood biochemical investigations and tumor markers is of important reference value for screening of patients with gastric cancer and can provide the basis for early treatment of the disease. With a larger trial, we would be able to make more definitive statements regarding the importance of these biochemical parameters and the proper timing for measurement. Future mechanistic studies are therefore necessary to establish whether serum LDH is a proxy of tumour growth and severity, which explains its association to cancer survival, or whether it is also involved in early carcinogenesis. Further research is needed to help planning the follow-up strategy using these biochemical indicators.

Ethical Clearance – Institutional Ethical Committee Clearance obtained.

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