INVESTIGATION OF GASTRIC CANCER PATIENTS BY TUMOR MARKERS AND TUMOR SUPPRESSOR MARKER IN IRAQ

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ABSTRACT

In comparison to other cancers, gastric cancer is the most frequent cancer in the world, particularly in Iraq, and it affects individuals aged 30 and up. Our research focuses on confirming malignant indicators, through the concentrations of carbohydrate antigen 72-4 (CA72-4), carbohydrate antigen 125 (CA125), Alp-fetoprotein (AFP), and Protein53 (P53), these markers were measured in the sera of both patients with gastric cancer and healthy group. Ninety patients with gastric cancer were selected from AL-Hussein Teaching Hospital of Kerbala and 100 healthy subjects represented as the control group, their ages were identical with the ages of patients. The clinical characteristics of patients were documented, which included age, smoking, family history, and obesity. Statistical analysis of the results showed that 60% of patients were aged (51-65) year and 40% were between the ages of (30-50) year.

Student’s t-test was used to analyze the results. The statistical results were documented a highly significant (P<0.000) increase in the level of CA72-4, CA125, and AFP. There also was a highly significant (P<0.01) increase in P53 level, compared with the healthy group. By using Pearson's correlation coefficient between parameters under study in gastric cancer patients, the results revealed a positive significant correlation between CA72-4 and CA125 (P<0.000, r=0.591), CA72-4 and AFP (P<0.01, r=0.360), CA72-4 and P53 (P<0.000, r=0.614), CA125 and AFP (P<0.000, r=0.654), CA125 and P53 (P<0.000, r=0.797).

The demographic study of patients which included age, smoking, family history, and obesity, the results were demonstrated a significant (P<0.05) increase in the level of CA72-4 in smoker patients, when compared with non-smoker patients, whereas there wasn't noticed any significant (P>0.05) in the other parameters under study in smoker patients with gastric cancer. The results didn’t show any significant variation (P>0.05) in levels of all parameters that used in the present research, with another clinical characteristics (age, family history, obesity) in gastric cancer patients.

Keywords: CA72-4, P53, Tumor Markers, Tumor supressor.

I. INTRODUCTION

Gastric cancer (GC) is globally the fifth most common cancer and third leading cause of cancer death after the breast, bladder, lung, and colon carcinoma [1]. During the last years, several biochemical markers of gastric carcinoma have been introduced. Most of these markers like carbohydrate antigen 72-4 (CA72-4), carbohydrate antigen 125 (CA125), Alpha fetoprotein (AFP), and tumor protein 53 (P53) were derived from increased tumor cell volume [2].

Tumor-associated glycoproteins (CA72-4, CA125,) found on the surface of many cancer cells including gastric, colon, lung, ovary, breast, and pancreatic cancer [3], while AFP was protein synthesized in the hepatic cells and used a tumor protein marker, which increased when found cellular tumor as a liver tumor and gastrointestinal tumors like gastric tumor [4].

Previous studies showed elevation of CA72-4 in the sera of up to 40% of patients with colorectal and 42.6% of patients with gastric cancer, with increased levels being significant correlated with advanced stages of disease [5].
CA125 has traditionally been identified as a particular biochemical marker for ovarian carcinomas and has been regarded as a diagnostic tool for gastric carcinoma. With peritoneal recurrence, CA125 is most often positive, and the value of CA125 in the assessment of peritoneal metastasis [6].

Elevated serum alpha-fetoprotein (AFP) levels in adults are considered abnormal. This parameter is used mostly in the diagnosis and follow-up of hepatocellular carcinomas and yolk sac tumors. Among the other rare tumors accompanied with elevated serum AFP levels, gastric cancer is the most common [7].

Protein 53 (P53) was a tumor antigen to host cellular mutations, and one of the common alterations observed in human tumors used a tumor suppressor, through suggests mechanism lead to regulate the cell cycle [8].

II. MATERIALS AND METHODS

Patients and control
This study included ninety patients with gastric carcinoma; those patients were enrolled from AL-Hussein Teaching Hospital of Kerbala in the period from April 2020 to January 2021, whose age ranges between (30-65) years. Blood samples of those patients were obtained from oncology unit, diagnosed as gastric cancer by the histopathological examination.

The Control group was consisted of 100 healthy subjects who were free from signs and symptoms of cancer, and whose ages were identical with the age of patients.

III. SPECIMEN COLLECTION
Trained nurses collected venous blood samples (5 ml) from each individual of both gastric cancer and healthy control. To each blood sample was used plain plastic tubes (5ml) for our parameters under study.

Disposable syringes and needles were used to collection the blood specimens. The blood samples of tumor marker studies were centrifuged at 3000 xg for 15 minute. A serum of these blood samples was taken with its tubes and put to freeze at -70 °C until the analysis.

Determination of Carbohydrate antige 72-4 (CA72-4)
Serum CA72-4 was identified using the enzyme-linked Immunosorbent Assay (ELISA) (Human alpha-fetoprotein ELISA package, CSB-E09411h, CUSABIO, China).

Determination of Carbohydrate antige 125 (CA125)
Serum CA125 was identified using the enzyme-linked Immunosorbent Assay (ELISA) (Human protein53 ELISA package, MBS3802444, Mybiosource, USA.).

Determination of Alpha-fetoprotein (AFP)
Serum AFP was identified using the enzyme-linked Immunosorbent Assay (ELISA) (Human alpha-fetoprotein ELISA package, CSB-E04770h, CUSABIO, China).

Determination of Protein 53 (P53)
Serum P53 was identified using the enzyme-linked Immunosorbent Assay (ELISA) (Human protein53 ELISA package, MBS824754, Mybiosource, USA.).

IV. STATISTICAL ANALYSIS
Student t-test was used to analyze the results. All of the data were expressed as mean ± standard error (Sd.E), P-value ≤ 0.05 was considered significant. Statistical analyses were conducted using SPSS 19.0 statistical software (SPSS).

V. RESULTS AND DISCUSSION
The results revealed a highly significant (P<0.01) increase in the concentration of serum tumor protein 53 (P53), compared with healthy group. In addition, there was a highly significant (P<0.000) increase in the concentration of serum alpha-fetoprotein (AFP), compared with healthy group (Table 1).
Table 1: The levels of parameters under study in patients with gastric cancer and control group.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Patients n=90 Mean±Sd.E</th>
<th>Control n=100 Mean±Sd.E</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA72-4 (U/ml)</td>
<td>83.67±15.67</td>
<td>2.10±0.141</td>
<td>0.000</td>
</tr>
<tr>
<td>CA125 (U/ml)</td>
<td>269.03±69.08</td>
<td>5.06±0.27</td>
<td>0.000</td>
</tr>
<tr>
<td>AFP (ng/ml)</td>
<td>9.41±0.09</td>
<td>8.46±0.05</td>
<td>0.000</td>
</tr>
<tr>
<td>P53 (μg/L)</td>
<td>301.34±62.60</td>
<td>85.82±3.62</td>
<td>0.008</td>
</tr>
</tbody>
</table>

Carbohydrate antigen 72-4 (CA72-4) is highly sensitive to gastric cancer, and the positive rate of serum CA72-4 in gastric cancer is reported to be 36% to 94%. And its specificity is also high, some of which even reach 100% [9]. Clinical studies have found that serum CA72-4 is lower after the resection of gastric cancer than that before operation, and there is a significant difference before and after operation. As a consequence, CA72-4 can be used to detect whether there are residual tumor cells after operation and judge the prognosis of gastric cancer [10]. Although more and more studies have pointed out the importance of CA72-4 in the prognosis of gastric cancer, there is a lack of evidence-based evidence.

Previous clinical trials revealed that serum CA 125 may be used as an indicator to detect the recurrence of gastric cancer, and predict the prognosis and poor biological behavior. The majority of studies on the association between CA 125 and gastric cancer suggest that elevated serum CA 125 is associated with peritoneal metastasis [11]. Farshad et al demonstrated that CA 125 is primarily distributed throughout the ovaries and fallopian tube epithelium; however, it is also identified in the peritoneum, pleura and pericardium of the mesothelial cells. The peritoneal metastasis in those tissues may be a result of peritoneal examination or adhesion, leading to CA 125 antigen content being increased significantly [12].

Present study, to Follow-up of AFP levels documented that the AFP in metastatic gastric cancer patients with elevated AFP levels may allow prediction of early treatment response and could be more useful than the carcinoembryonic antigen (CEA) marker for follow-up in response evaluation [13].

The tumor suppressor gene p53 is one of the most frequently mutated genes in human cancers, and p53 mutations occur in 0 to 77% of stomach cancers. Mutation of p53 has been observed starting at the early stages of gastric cancer and this frequency increases as the malignancy progresses [14].

Pearson's Correlation Coefficient was used to mean the correlation between parameters in patients group. The results revealed a positive significant correlation between CA72-4 and CA125 (P<0.000, r=0.591), CA72-4 and AFP (P<0.01, r=0.360), CA72-4 and P53 (P<0.000, r=0.614), CA125 and AFP (P<0.000, r=0.654), CA125 and P53 (P<0.000, r=0.797) (Table 2).
Table 2. The correlations between parameters under study in gastric cancer patients.

<table>
<thead>
<tr>
<th>Parameter 1</th>
<th>Parameter 2</th>
<th>n</th>
<th>(r)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA72-4</td>
<td>CA125</td>
<td>90</td>
<td>0.591*</td>
<td>0.000</td>
</tr>
<tr>
<td>CA72-4</td>
<td>AFP</td>
<td>90</td>
<td>0.360*</td>
<td>0.014</td>
</tr>
<tr>
<td>CA72-4</td>
<td>P53</td>
<td>90</td>
<td>0.614**</td>
<td>0.000</td>
</tr>
<tr>
<td>CA125</td>
<td>AFP</td>
<td>90</td>
<td>0.654**</td>
<td>0.000</td>
</tr>
<tr>
<td>CA125</td>
<td>P53</td>
<td>90</td>
<td>0.797**</td>
<td>0.000</td>
</tr>
</tbody>
</table>

*Correlation is significant at the 0.05 level.
**Correlation is significant at the 0.01 level.

In our study, the correlations between tumor markers levels during clinical outcomes in patients with locally or metastatic gastric cancer showed strongly correlation. Gastric cancer patients with metastatic cancer have higher levels of CA72-4, CA125 and AFP than those with localized cancer and benign tumor [15]. The study of Minxia, et al. (2020) detected that serum high levels of CA72-4 and AFP results may provide valuable additional indicators of the cancer which metastasis to the bone in untreated patients, and in monitoring the efficacy of therapy [10]. These mean, that higher pretreatment serum levels of CA72-4, AFP and P53 are good prognostic factors for patients with metastatic gastric cancer on hormonal treatment, irrespective of tumor grading [16].

Demographic study

Age factor

In this study, the patients with gastric cancer were categorized into two groups according to their age. Group 1 consists of 36 patients (40%) with ages between 30-50 years. Group 2 consist of 54 patients (60%) with ages between 51-65 years (Figure 1). The statistical analysis of results did not show any significant variation (P>0.05) in all parameters under study between the two age groups (Table 3).
Table 3: The levels of parameters under study in patients with gastric cancer in two age groups.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Age(30-50) n=36 Mean±Sd.E</th>
<th>Age(51-65) n=54 Mean±Sd.E</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA72-4 (U/ml)</td>
<td>74.65±19.08</td>
<td>90.02±23.31</td>
<td>0.612</td>
</tr>
<tr>
<td>CA125 (U/ml)</td>
<td>318.23±112.53</td>
<td>234.40±88.26</td>
<td>0.561</td>
</tr>
<tr>
<td>AFP (ng/ml)</td>
<td>226.50±34.58</td>
<td>354.11±103.54</td>
<td>0.251</td>
</tr>
<tr>
<td>P53 (μg/L)</td>
<td>9.47±0.16</td>
<td>9.37±0.11</td>
<td>0.629</td>
</tr>
</tbody>
</table>

Prashanth, *et al.* (2019) revealed the older men are more likely to be diagnosed with gastric cancer. Although only 1 in 10,000 men under age 40 will be diagnosed, the rate shoots up to 1 in 38 for ages 40 to 59, and 1 in 14 for ages 60 to 69 [17].

In fact, more than 65% of all gastric cancers are diagnosed in persons over the age of 50 year. The average age at diagnosis of gastric cancer in the United States was 65 year. After that age, the chance of developing gastric cancer becomes more common than any other cancer in men or women [18].

**Smoking factor**

In this study, patients with gastric cancer were classified into two groups, smokers 30 case (33%), and non-smokers 60 case (67%) (Figure 2). The results did not show a significant (P˃0.05) different in the concentration of all parameters under study between smoker and non-smoker patients, except there was significant (P˂0.05) increase in concentration of serum CA72-4, in smoker patients compared with non-smoker patients (Table 4).

![Figure 2: The percentage of smokers and non-smokers patients.](image-url)
Table 4: The levels of parameters under study in smoker and non-smoker patients.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Smoker n=33% Mean±Sd.E</th>
<th>Non Smoker n=67% Mean±Sd.E</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA124 (U/ml)</td>
<td>33.33±17.61</td>
<td>95.91±18.54</td>
<td>0.021</td>
</tr>
<tr>
<td>CA125 (U/ml)</td>
<td>104.01±81.49</td>
<td>309.17±82.63</td>
<td>0.089</td>
</tr>
<tr>
<td>AFP (ng/ml)</td>
<td>197.47±30.43</td>
<td>326.60±77.14</td>
<td>0.127</td>
</tr>
<tr>
<td>P53 (μg/L)</td>
<td>9.36±0.15</td>
<td>9.42±0.11</td>
<td>0.765</td>
</tr>
</tbody>
</table>

Currently, there was no strong evidence that smoking, vasectomy, obesity or high alcohol intakes are risk factors in the development of gastric cancer [19]. Results of the different epidemiological studies are controversial, probably because of differences in sampling and methods of analysis. In most cases only insufficient marginal differences can be established [20].

VI. CONCLUSION

Gastric cancer is associated with elevated carbohydrate antigen 72-4 (CA72-4), carbohydrate antigen 125 (CA125), Alpha-fetoprotein (AFP), and tumor protein 53 (P53). In addition, the gastric cancer is starts in middle ages in the most cases, that is about 50 years and over. Family history is one of risk factors that associated with gastric cancer.

REFERENCES