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COMPARISON OF CEA AND CA 19-9 WITH CA 72-4 IN PATIENTS WITH UPPER GASTROINTESTINAL CARCINOMAS IN LOCAL POPULATION

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ABSTRACT

Introduction: *Gastrointestinal carcinomas are amongst the most common malignancy showing an annual increase globally. In our population, there is an increase in GIT carcinomas over the years and these are occurring at a much younger age. Tumour markers are molecular substances produced by all tumour cells which are excreted in body fluids or present on the surface of the cells. CEA, CA 19-9 and CA 72-4 are tumour markers for GIT carcinomas.* ***Materials and Methods:*** *The study included patients of upper GIT carcinoma and controls of both sexes and all ages. Each category included about 30 blood samples. Serum of each sample was evaluated for tumour markers CEA, CA 19-9 and CA 72-4. The estimations were made by using ELISA / EIA. The t-test and ANOVA were performed for comparison of means, specificity and sensitivity of each marker were also calculated.* ***Results*** *showed that in our population GIT carcinoma is common in younger age group. Sensitivity of CEA, CA 19-9 and CA 72-4 is 63.33%, 50% and 63.33% respectively whereas specificity of these markers are 60%, 93.33% and 100% respectively in upper GIT carcinoma. CA 19-9 is tumour marker of choice for pancreatic carcinoma and CA 72-4 for gastric carcinoma.*

INTRODUCTION

Gastrointestinal carcinomas are amongst the most common malignancy showing an annual increase globally.[1] In our population, there is an increase in GIT carcinomas over the years, from 9% in 1961 to 17% in 1992 with respect to all carcinomas reported. It was observed that GIT carcinomas have increased significantly over the years in our local population and are occurring at a much younger age, as compared to western population, i.e., 74% occurring between 35-64 years of age.[1] There are a few studies carried out in other parts of world regarding the role of tumour markers in the GIT carcinomas.[2-3] They are seen in fluids and tissues.[4] CEA is a high-molecular-weight glycoprotein present in colonic adenocarcinoma and fetal gut.[5,6] An increased value of CEA has been observed in cancer of colon, rectum, lung, breast, liver, pancreas, prostate, stomach, and ovary. It is also elevated in benign liver, gastric, intestinal and breast diseases, pulmonary infection, emphysema, and renal failure.[5] CA 19-9 is a carbohydrate antigen occurring as a glycolipid in tissues and as a mucin-type glycoprotein in serum. It is synthesized by normal human pancreatic and biliary ductular cells and by gastric, colonic, endometrial, and salivary epithelia. CA 19-9 is a marker for both pancreatic and colorectal carcinoma.[7]

CA 72-4 is an antigenic tumour associated glycoprotein (TAG-72) that reacts with mouse monoclonal antibody B 72.3, directed against the membrane component fraction of mammary carcinoma. It metastasises in the liver, and mouse monoclonal antibody CC 49 that is extracted and refined from cultured colon cancer cells LS-174T3. Preoperative serum concentrations of CA 72-4, which tend to be higher with increased dissemination of gastric cancer cells, may be a more reliable tumour marker than carcinoembryonic antigen (CEA).[5] CA 72-4 is a marker for carcinomas of the gastrointestinal tract and of the ovary.[8] The measurements of the serum marker CA 72-4 were useful and correlated well with disease stage and activity. The CA 72-4 antigen was distinct from CEA and has been purified and characterized as a mucin-like molecule on the basis of its high molecular weight, resistance to chondroitinase digestion, density determination, the presence of blood group-related oligosaccharides, and sensitivity to shearing into lower molecular weight forms.[9]

MATERIALS AND METHODS

The study included controls and patients with upper GIT. In each category 30 blood samples were included. Upper GIT carcinoma was further divided into oesophagus, stomach and pancreatic carcinomas. This study has been performed in the University of Health Sciences, Lahore and sample collection was carried out in Services Hospital Lahore, Jinnah Hospital Lahore and Sheikh Zayed Hospital Lahore. All patients of either sex, any age group with clinical

diagnosis of GIT carcinoma and normal healthy matching control group were included in the study. Patients who did not survive after surgery were excluded and the those having severe co-morbid diseases like severe cirrhosis and uncontrolled diabetes were excluded.

Blood samples were collected in 5 ml disposable syringe and were emptied into red top evacuated tubes. Serum was separated from the blood by allowing it to clot and centrifuged at 3000 rpm for 10 minutes. The serum of each sample was divided into 3 portions and stored in Eppendorf tubes with cap at -20°C. Serum of each sample was evaluated for tumour markers CEA, CA19-9 and CA 72-4. The estimations were carried out by using ELISA/EIA. The kits were CEA Enzyme immunoassay test kit (Bio-Check Enzyme Immunoassay), CA19-9 Enzyme immunoassay test kit (BioCheck Enzyme Immunoassay) and CA72-4 Enzyme-Linked Immunosorbent Assay (ELISA) kit (DRG Diagnostics). The t-test and ANOVA were performed for comparison of means and specificity and sensitivity of each marker were also calculated.

RESULTS

The present study included 60 males and females of different ages selected from Services Hospital, Sheikh Zayed and Jinnah Hospital, Lahore.

Thirty patients were diagnosed and confirmed cases of upper GIT carcinomas. They were further grouped under oesophageal, stomach and pancreatic carcinomas. Thirty healthy males and females of same ages were included as controls.

The ages of the patients were categorised into groups as 20-29, 30-39, 40-49,50-59, 60-69 and more than or equal to 70 years. The frequencies of upper GIT carcinoma in these age groups are given in table 1. The frequencies of individual carcinomas including those of oesophagus carcinoma, stomach carcinoma and pancreatic carcinomas are shown in table 2. Significant difference was observed between different carcinomas and CEA levels after applying ANOVA. p - value < 0.003 (Table 3). After applying Post Hoc Tukey Test no significant difference was observed among

Table 1: *Frequency distribution of upper GIT carcinomas.*

Age		Upper GIT Carcinoma
20 - 29	Count	3
	% of Total	4.8%
30 – 39	Count	9
	% of Total	14.5%
40 – 49	Count	8
	% of Total	12.9%
50 – 59	Count	3
	% of Total	4.8%
60 - 69	Count	3
	% of Total	4.8%
>= 70	Count	4
	% of Total	6.5%
Total	Count	30
	% of Total	48.4%

Table 2: *Frequency distribution in subgroups of upper GIT carcinomas.*

Age		GROUP		
		Oesophagus carcinoma	Stomach carcinoma	Pancreatic carcinoma
20 – 29	Count	1	0	2
	% of Total	1.6%	.0%	3.2%
30 – 39	Count	4	4	1
	% of Total	6.5%	6.5%	1.6%
40 – 49	Count	6	2	0
	% of Total	9.7%	3.2%	.0%
50 – 59	Count	1	1	1
	% of Total	1.6%	1.6%	1.6%
60 – 69	Count	0	1	2
	% of Total	.0%	1.6%	3.2%
>= 70	Count	0	0	4
	% of Total	.0%	.0%	6.5%
Total	Count	12	8	10
	% of Total	19.4%	12.9%	16.1%

other groups (Table 4). Significant diffe-rence was observed between various carci-nomas and CA 19-9 levels after applying ANOVA. p-value < 0.001 (Table 5). After applying Post Hoc Tukey Test, significant difference was observed between oesopha-gus and pancreatic carcinomas (p-value = 0.046), stomach and pancreatic carcino-ma (p-value = 0.017) and pancreatic carci-noma and control (p-value = 0.000) by using CA 19-9 as tumour marker. On the other hand no significant difference was observed among other groups (Table 6). No significant difference was observed between various carcinomas and CA 72-4 levels after applying ANOVA. p-value > 0.539 (Table 7). After applying Post Hoc Tukey Test, no significant difference was observed between all the groups by using CA 72-4 as tumour marker (Tab-le 8).

The sensitivity, specificity, diagnostic accuracy, positive predictive value and negative predictive values were calculated. Tumour marker CEA has the sensitivity of 63.33%, specificity of 60%, diagnostic accuracy of 61.66%, PPV 70.37% & NPV 62.06% for upper GIT carcinoma. CA 19-9 has the sensitivity of 50%, specificity of 93.33%, diagnostic accuracy of 71%, positive predictive value of 88.23% and negative predictive value of 65.11% for upper GIT carcinomas. CA 72-4 has the sensitivity of 63.33%, specificity of 100%, diagnostic accuracy of 81.66%, positive predictive value of 100% and negative predictive value of 73.17% for upper GIT carcinoma (Table 9). Upper GIT included oesophagus, stomach and pancreatic carcinoma.

Table 3: *Frequency distribution of CEA in different types of GIT carcinomas and control.*

	Oesophagus carcinoma Mean ± S.D	Stomach carcinoma Mean ± S.D	Pancreatic carcinoma Mean ± S.D	Control Mean ± S.D	P-value
CEA	6.236 ±7.564	5.469 ± 3.054	55.331 ± 63.142	7.741 ± 11.370	0.003

Table 4: *Frequency distribution of CA 72-4 in different types of GIT carcinomas and control.*

	Oesophagus carcinoma Mean ± S.D	Stomach carcinoma Mean ± S.D	Pancreatic carcinoma Mean ± S.D	Control Mean ± S.D	p-value
CA72-4	5.805 ± 4.240	8.749 ± 8.353	9.290 ± 12.878	0.482 ± 0.420	0.539

Table 5: *Distribution of cases by relative diagnostic values in Upper GIT carcinoma.*

	CEA	CA19-9	CA72-4
Sensitivity	63.33%	50%	63.33%
Specificity	60%	93.33%	100%
Diagnostic accuracy	61.66%	71.66%	81.66%
P.P.V	70.37%	88.23%	100%
N.P.V	62.06%	65.11%	73.17%

Table 6: *Distribution of cases by relative diagnostic values in Oesophageal carcinoma*

	CEA	CA19-9	CA72-4
Sensitivity	41.66%	33.33%	50%
Specificity	60%	93.33%	100%
Diagnostic accuracy	54.76%	76.1%	86%
P.P.V	29.41%	66.66%	100%
N.P.V	72%	77.77%	83.33%

Table 7: *Distribution of cases by relative diagnostic values in gastric carcinoma.*

	CEA	CA19-9	CA72-4

Sensitivity	50%	12.5%	75%
Specificity	60%	93.33%	100%
Diagnostic accuracy	58%	76.31%	94.73%
P.P.V	25%	33.33%	100%
N.P.V	81.81%	80%	93.75%

Their specificity, sensitivity, diagnostic accuracy, PPV and NPV were given in tables 10, 11 and 12.

Table 8: *Distribution of cases by relative diagnostic values in Pancreatic carcinoma.*

	CEA	CA19-9	CA72-4
Sensitivity	100%	100%	70%
Specificity	60%	93.33%	100%
Diagnostic accuracy	70%	95%	92.5%
P.P.V	45.45%	83.33%	100%
N.P.P	100%	100%	90.90%

DISCUSSION

Thirty patients were diagnosed and confirmed as cases of upper GIT carcinoma. Thirty healthy males and females of same ages were included as controls. The study showed that in age group between 30-40 upper GIT carcinoma is very high. Oesophagus and stomach carcinomas are high in age group 30-40. Pancreatic carcinoma is higher in age group 70 and above. The sensitivity of CEA, CA 19-9 and CA 72-4 in upper GIT Carcinoma is 63.33%, 50% & 63.33% respectively whereas specificity of the above mentioned tumour markers is 60%, 93.33% and 100% (Table 9). Hence, CA 19-9 and CA 72-4 are specific for upper GIT carcinomas.

Among these GIT malignancies, the sensitivity of CEA, CA 19-9 and CA 72-4 in oesophageal carcinoma is 41.66%, 33.33% and 50% respectively, and the specificity of the above mentioned tumour markers is 60%, 93.33% and 100% respectively (Table 10). Hence, CA 19-9 and CA 72-4 are specific for upper GIT carcinomas.

In gastric carcinoma CEA, CA 19-9 and CA 72-4 have sensitivity of 50%, 12.5% and 75% respectively. While specificity of above mentioned tumour markers is 60%, 99.33% and 94.73% respectively (Table 11). Hence, CA 72-4 is both sensitive and specific for stomach carcinoma.

For gastric carcinoma, CA 72-4 appeared the most sensitive tumour marker with a specificity of 78.9% and a diagnostic accuracy of 75.4%.[10] CA 72-4 showed high sensitivity and specificity for the management of GIT carcinomas,[11-14] and have prognostic value for pancreatic carcinoma the sensitivity of CEA, CA 19-9 and CA 72-4 is 100%, 100% and 70% respectively, whereas the specificity of above mentioned tumour markers is 60%, 93.33% and 100% respectively (Table 12). Hence, our study showed that CA 19-9 is both specific and sensitive for pancreatic carcinoma. It is the diagnostic test for pancreatic carcinoma.[15]

In serodiagnostic evaluations relating to pancreatic carcinoma, CA 19-9 proved superior to CA 72-4 and CEA with sensitivity: 79.5 vs. 56.5 and 62.5% and specificity: 84.1 vs. 77.9 and 77.2%).[11] Patai et al discussed that the specificity of CA 19-9 was 89.5% while sensitivity was 91.7%.[16]

It is **concluded** from this study that in our population GIT carcinomas are common in younger age group i.e., below 30. CEA is the sensitive test for the diagnosis of GIT carcinoma while CA 19-9 and CA 72-4 are the specific test for GIT carcinoma. When individual carcinomas are studied, CA 19-9 is the tumour marker of choice in pancreatic carcinoma and also has diagnostic value. CA 72-4 is the tumour marker of choice for gastric carcinoma.

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