

## TO ESTIMATE THE LEVELS OF CA19-9 AND ITS SIGNIFICANCE IN DIAGNOSIS AND TREATMENT OF PANCREATICOBILIARY AND GASTROINTESTINAL MALIGNANCIES

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### ABSTRACT

**Objective:** This study was designed and conducted to establish the relationship of biomarker CA19-9 levels in pancreaticobiliary and gastrointestinal malignancies.

**Methods:** 50 patients with confirmed diagnosis of pancreaticobiliary and gastrointestinal malignancies and 30 age and gender matched controls were included in the study. Serum values of CA19-9 were determined in patients before surgery and chemotherapy.

**Results:** In our present study, maximum number of patients were in the age group of 51–60 years. Mean levels of serum CA19-9 in patients (n=50) are  $146.28 \pm 156.87$  U/mL. Total patients (n=50), in 19 patients CA19-9 levels were  $\leq 37$  U/mL and in 31 patients CA19-9 levels were  $>37$  U/mL. CA19-9 levels were highest in pancreatic and cholangiocarcinoma.

**Conclusion:** High sensitivity and specificity of CA19-9 in pancreatic and biliary tract tumors identified CA19-9 as a best validated biomarker.

**Keywords:** CA19-9, Pancreaticobiliary carcinoma, Metastatic disease.

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### INTRODUCTION

The past decade has seen a growing understanding of molecular pathology of tumors. Knowledge of a tumor's molecular characteristics plays a key role in the development of markers that aid in the diagnosis, management, and prediction of outcome of a neoplastic condition. Definitive treatment of malignancy still remains elusive. Concerted efforts have been made to understand incidence and distribution of various malignancies, worldwide, and region wise.

Pancreatic and biliary tract cancers are aggressive malignancies which are present with metastatic diseases [1]. Pancreatic cancer results from the successive accumulation of gene mutations [2]. Interactions between pancreatic cancer cells and stromal cells promote tumor growth, invasion, metastasis, and chemoresistance [3]. Biliary tract cancer is a heterogeneous type of cancer [4] diagnosed in the advanced and metastatic stages [5].

Biomarkers are biochemical substances elaborated by tumor cells. Evaluation of tumor markers can be valuable aid in diagnosis, prognosis, staging, and in monitoring the growth of tumor [6]. Tumor markers are potentially used in screening for early malignancy or may help in the differential diagnosis of benign and malignant disease [7]. Elevated levels of tumor markers could signalize advanced stage of the disease [8].

Carbohydrate Antigen 19-9 (CA19-9) is a glycoprotein used currently in the diagnosis and follow-up of gastrointestinal tumors [9]. CA19-9 is regularly expressed on cells of the pancreaticobiliary system and is initially detected by the monoclonal antibody 19-9 [10].

Malignant transformation and progression in tumors are closely related to alterations in cell-surface carbohydrate antigens (CAs) with frequent aberrant glycosylation [11]. Selectins and their carbohydrate ligands can thus play an important role in the selective homing of tumor cells during metastasis [12].

The utility of CA19-9 in assessing the resectability of pancreatic cancer is based on the correlation between CA19-9 levels and tumor stage [13]. CA 19-9, as a ligand of E-selectin and an intercellular adhesion molecule, plays a crucial role in intercellular adhesion of tumor cells to vascular endothelial cells and then contributes to tumor invasion and metastasis. Cells expressing CA19-9 have a greater capacity of invasion and metastasis. CA19-9 may be drained by thoracic duct of lymphatic system through node metastasis. Thus, elevated level of CA19-9 prompts the presence of micrometastases which can lead to subsequent metastasis [14].

CA 19-9 decline is a useful measure of the degree of response to treatment. Normalization of CA 19-9 levels likely indicates response of both the primary tumor as well as subclinical micrometastases [15]. CA19-9 kinetics during chemotherapy contributes to predict tumor response as well as survival [16].

### Aim

The aim of the study was to estimate the CA 19-9 levels in GIT cancers including pancreaticobiliary cancers and also to analyze the significance of CA 19-9 levels in the treatment and monitoring patients.

### METHODS

50 patients with confirmed diagnosis of pancreaticobiliary and gastrointestinal malignancies and 30 age- and gender-matched controls were included in the study, in the Department of Biochemistry referred by Department of Surgery, Rajindra Hospital, Patiala. Patients were explained the study and consent was obtained. Patient's information was collected such as age, sex, chemotherapy, smoking status, and diabetic status. Patients with history of benign diseases and other malignancies were excluded from the study. Serum values of CA19-9 were determined in patients before surgery and chemotherapy. Pre-operative serum levels of CA19-9 were compared statistically using pair t test and Chi-square test in SPSS software.

### OBSERVATION AND RESULTS

Age-wise distribution of patients included in the study (n=50) is shown in Table 1.

Pancreaticobiliary and gastrointestinal malignancies have been diagnosed in almost every group. In the present study, maximum number of patients was in the age group of 51–60 years.

Mean levels of serum CA19-9 in patients (n=50) with pancreaticobiliary and gastrointestinal malignancies and in controls (n=30) are shown in Table 2.

Distribution of patients according to diagnosis of CA19-9 levels is shown in Table 3. In our present study, of total patients (n=50), in 19 patients CA19-9 levels were  $\leq 37$  U/mL, and in 31 patients CA19-9 levels were  $>37$  U/mL.

**Table 1: Age-wise distribution**

Age group (years)	Cases, frequency (%)
$\leq 30$	0
31–40	7 (14.0)
41–50	8 (16.0)
51–60	18 (36.0)
$>60$	17 (34.0)
Total	50 (100.0)

**Table 2: Mean carbohydrate antigen 19-9 levels**

Parameter	Study group	Mean $\pm$ SD (U/ml)	p	Significance
CA 19-9 levels	Cases (n=50)	146.28 $\pm$ 156.87	$<0.001$	HS
	Controls (n=30)	12.46 $\pm$ 6.23		

SD: Standard deviation, HS: Highly significant, CA: Carbohydrate antigen

**Table 3: Distribution of patients according to the diagnosis of carbohydrate antigen 19-9 levels**

Malignancy	CA 19-9 $\leq 37$ (U/ml), n (%)	CA 19-9 $>37$ (U/ml), n (%)	Total
Pancreatic	1 (25.0)	3 (75.0)	4
Gall bladder	4 (80.0)	1 (20.0)	5
Cholangiocarcinoma	0	3 (100.0)	3
Hepatocellular	1 (25.0)	3 (75.0)	4
Gastric	2 (20.0)	8 (80.0)	10
Colorectal	9 (42.9)	12 (57.1)	21
Esophageal	2 (66.7)	1 (33.3)	3
Total	19 (38.0)	31 (62.0)	50

CA: Carbohydrate antigen

**Table 4: Mean levels of carbohydrate antigen 19-9 in different malignancies**

Malignancies	n	Minimum (U/ml)	Maximum (U/ml)	Mean $\pm$ SD (U/ml)	p	Significance
Pancreatic	4	17.41	600.00	324.94 $\pm$ 318.70	$<0.001$	HS
Gall bladder	5	16.72	132.50	46.15 $\pm$ 48.917		
Cholangiocarcinoma	3	123.30	600.00	339.86 $\pm$ 241.31		
Hepatocellular	4	24.38	276.70	177.62 $\pm$ 109.43		
Gastric	10	9.96	329.90	173.97 $\pm$ 122.60		
Colorectal	21	5.198	342.00	105.31 $\pm$ 106.78		
Esophageal	3	10.83	57.35	34.13 $\pm$ 23.26		

SD: Standard deviation, HS: Highly significant

**Table 5: Comparison of routine biochemical investigations of study and control group**

Parameter	Mean $\pm$ SD		p	Significance
	Study group (n=50)	Controls group (n=30)		
Blood urea (mg%)	44.72 $\pm$ 29.70	32.77 $\pm$ 8.148	0.035	S
Serum creatinine (mg%)	1.202 $\pm$ 0.688	0.836 $\pm$ 0.167	0.006	S
Serum amylase (U/L)	78.46 $\pm$ 36.63	53.10 $\pm$ 11.874	$<0.001$	HS

SD: Standard deviation, S: Significant, HS: Highly significant

Mean levels of CA19-9 in patients according to diagnosis of different malignancies are shown in Table 4. CA19-9 levels were highest in pancreatic and cholangiocarcinoma.

Comparison of routine biochemical investigations of study and control group is shown in Table 5. B. Urea and S. creatinine levels were significant and S. amylase level is highly significant in study and control group.

There was statistically significant increase in mean serum CA19-9 levels in pre-operative pancreaticobiliary and gastrointestinal malignancies.

## DISCUSSION

The present study was conducted at Government Medical College and Rajindra Hospital Patiala, India. This study has established that serum levels of CA19-9 increase in cases of pancreaticobiliary and gastrointestinal malignancies.

Tsen *et al.* studied elevated levels of CA 19-9 in biliary pathology [17].

Sachan *et al.* in their study concluded that CA19-9 is the most commonly used tumor marker in gallbladder cancer. Raised CA19-9 predicts metastatic disease in patients with gallbladder cancer and is used in predicting tumor burden and recurrence [18].

Luo *et al.* in their study concluded that carbohydrate antigen 19-9 (CA19-9) is the best validated biomarker and an indicator of aberrant glycosylation in pancreatic cancer and the sensitivity is approximately 80% [13].

Yamashita *et al.* in their study concluded that pre CA19-9 is useful in predicting patient's prognosis in Stage IV CRC patients. A multivariate prognostic analysis also revealed that pre CA19-9 is an independent prognostic factor in stage IV CRC [19].

Gur *et al.* conducted their study on tumor markers and biochemical parameters and concluded that levels of S. creatinine and S. amylase significantly increased in gastrointestinal malignancies [20].

Findings of our present study are also on the same lines as above. Production and secretion of CA19-9 from malignant cells is considered to be responsible for the elevated serum CA19-9 levels found in malignancy. Leakage of condensed CA19-9 due to biliary tract obstruction from bile into blood circulation. Enhanced production of CA19-9 in the bile duct epithelium and the mucosa of the gall bladder induced by the inflammatory process. Our present study findings are also same on biochemical investigations as there is significant increase in levels of S. creatinine and S. amylase.

The mean S. creatinine levels were high in our study group which is probably due to intake of drugs by patients which are nephrotoxic. The mean S. amylase levels were high in our study group as ascitic and pleural fluids may contain amylase as a result of the presence of tumor or pancreatitis. Biliary tract disease caused up to four-fold elevation of serum amylase activity as a result of either primary or secondary pancreatic involvement.

## CONCLUSIONS

Role of biomarkers in malignancies have been accepted and is widely used. CA19-9 has been identified as the best validated biomarker in pancreaticobiliary and gastrointestinal malignancies. The serum CA19-9 levels were significantly higher. CA19-9 functions as a biomarker, predictor, and promoter in pancreatic cancer. CA19-9 has a relatively high sensitivity and specificity for pancreatic and biliary tract tumors. Pre- and post-operative CA19-9 levels are relevant predictive markers of survival in patients with resectable cholangiocarcinoma. CA19-9 kinetics during chemotherapy contributed to predict tumor response as well as survival.

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## CONFLICT OF INTEREST/FUNDING

None.

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