



DIAGNOSTIC AND PROGNOSTIC SIGNIFICANCE OF CA19.9 IN PANCREATIC AND GALL BLADDER MALIGNANCIES.

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ABSTRACT **Introduction:** Carbohydrate antigen 19-9 or sialyl Lewis x is a tumor marker predominantly associated with pancreatic, gall bladder, gastric and colorectal cancers which are collectively classified as GI malignancies. CA 19-9 is presently the most clinically useful serological marker for pancreatic cancer. It has been shown that a persistent elevation in serum CA19-9 value following treatment may be indicative of occult metastatic and/or residual disease.

Materials And Methods: The present study was Retrospective, observational, analytical type done in Department of Pathology at a tertiary care center. Estimation of serum CA 19.9 level was done by using Indirect Sandwich Enzyme Linked Immunosorbent Assay (ELISA).

Results: 29 sample were received out of which 14 cases were followed up postoperatively. The sensitivity and specificity of CA 19-9 in diagnosing Pancreatic adenocarcinoma is 87.50% and 90.00% respectively. The sensitivity and specificity of CA 19-9 in diagnosing cholangiocarcinoma is 80% and 66.67% respectively. The sensitivity and specificity of CA 19-9 in diagnosing periampullary carcinoma is 70% and 86.67% respectively.

Conclusion: CA 19-9 values in normal individual is < 37 U/ml. Values >37 U/ml are considered abnormal. Higher the grade or stage of the tumor, higher is the value of serum CA 19-9. Elevated level of CA 19-9 is associated with higher age group, male, sex, higher histological grade, high TNM staging and metastasis. A persistently rising serum CA 19-9 value may be associated with progressive malignant disease and poor therapeutic response. A declining CA 19-9 value may be indicative of a favorable prognosis and good response to treatment.

KEYWORDS : Pancreatic carcinoma, Gallbladder carcinoma, Periampullary carcinoma, CA 19.9.

INTRODUCTION

The CA 19-9 antigen is a sialylated derivative of the Le^x antigen related to the Lewis (Le) blood group system¹⁵. Healthy men and women are expected to have CA19-9 assay values below 37 U/ml⁶⁻¹¹. In a significant number of GI malignancies, CA 19-9 levels are elevated above 37 U/ml. This is particularly pronounced in pancreatic and gall bladder cancer patients, followed by gastric and colorectal cancer patients⁶⁻¹¹. Sensitivity of CA 19-9 is moderate in early stage disease. The important feature of CA 19-9 assays is high specificity. It is useful in assisting diagnosis GI cancers and in assessing prognosis GI cancers^{11,12}. Pre-operative gastrointestinal cancer patients with CA 19-9 greater than 1000 kU/L have a poorer outcome than those with lower levels. Post-operative CA19-9 <200kU/L, and a post-operative decrease in CA 19-9 by >200 kU/L, are both indicators of a good outcome. Serial measurement of CA 19-9 can detect recurrent or metastatic GI cancer several months before it is clinical or radiological evident^{11,12}. CA 19-9 may be used alongside imaging to monitor response to treatment, in particular palliative chemotherapy.

Currently the most commonly used tumor marker for cholangiocarcinoma is CA 19-9. The use of a CA 19-9 level cutoff value of greater than 129 U/mL was shown to result in a sensitivity of 78.6% and a specificity of 98.5%.

Primary sclerosing cholangitis (PSC) predisposes to the development of cholangiocarcinoma, a usually fatal complication that is difficult to diagnose. Serum concentrations of CA 19-9, a tumor-associated antigen, are frequently increased in patients with only cholangiocarcinoma. The measurement of serum concentrations of CA 19-9 is a promising test for detecting cholangiocarcinoma in patients with PSC.

Besides its role in gastrointestinal cancer, elevation of CA 19-9 levels can also be seen in healthy individuals, in benign conditions, and in other malignant conditions. However, CA 19-9 levels tend to remain relatively stable over time in benign conditions. Malignant conditions include Primarily pancreatic carcinoma, cholangiocarcinoma, adenocarcinoma colon and gastric carcinoma. Also in hepatocellular carcinoma, breast, ovarian and lung carcinoma. Benign conditions include Acute and Chronic Pancreatitis, Cholecystitis, Cirrhosis, Chronic and Alcoholic Hepatitis, Acute hepatic necrosis, Gallstones, Cholestasis of any cause. Other condition include Lung disorders (cystic fibrosis, pneumonia, tuberculosis), Pelvic Inflammatory Disease, Hashimoto's Thyroiditis, Rheumatoid Arthritis, Renal Failure, Systemic Lupus Erythematosus (SLE).

AIMS AND OBJECTIVES

To establish diagnostic and prognostic role of CA 19.9 in Pancreatic and Gall bladder Malignancies and to study its role in monitoring.

MATERIALS AND METHOD

Patient's serum was taken as sample. Estimation of serum CA19.9 was done by using ELISA method which is Enzyme immunoassay for the quantitative determination of serum CA19.9.

Calbiotech –ELISA kit was used. Robonik wash well and read well-ELISA instrument were used. Study was done by Indirect Sandwich ELISA method.

Study Duration: Feb 2019-Feb 2021

Sample Size: Total 29 samples of CA19.9 were studied.

OBSERVATIONS AND RESULTS

Total numbers of cases of studied were 29. The cases were of patients admitted to various departments in tertiary care hospital. Mainly the patients were from Radiology, Surgery and Medicine department.

The patients included were those suspected of having gastro-intestinal malignancy like pancreatic carcinoma, cholangiocarcinoma and periampullary carcinoma. Pre-operative CA 19-9 was measured in every case for the purpose of diagnosis in some cases, post-operative CA 19-9 was measured and the patients was followed up for the length of the study of determine the prognosis and survival rate. Pre-operative CA 19-9 was measured before operation or at the time of taking fine needle aspiration. Post-treatment values were measured approximately 3 month after surgery or after completion of 3 cycle of chemotherapy/radiotherapy. Out of 29 patients studied, 15 patients had a regular follow up and 14 patients it was not possible to follow them up because of lack of communication or early death post-operatively.

Out of 29 cases studied, 3 cases were in the age group of 20 – 39 years. Maximum number of cases was in between 40 to 59 years that is 16 cases. Rest of the cases were in the age group more than 60 years. Out of all tumors, 17 cases occurred in males while 12 cases occurs in females giving a M:F ratio of 1.4:1.

Total 14 cases of pancreatic lesions were considered which included 10 cases of pancreatic ductal adenocarcinoma, 2 cases of acute pancreatitis, 1 case of mucinous cystadenoma of pancreas and 1 case of serous cystadenoma of pancreas.

RELATIONSHIP BETWEEN CLINOPATHOLOGICAL FACTORS AND CA 19-9 VALUES IN PANCREATIC LESIONS/ PANCREATITIS

SR. NO.	CLINOPATHOLOGICAL FACTORS	NUMBER	CA 19-9 (MEAN)	CA 19-9 (MEDIAN)
1	Age : (N=14)			
	20 – 39 yrs	2(14.2%)	289.63	250.9
	40-59 yrs	7(50%)	232.03	178.8
	> 60 yrs	5(35.7%)	350.20	350.2
2	Sex: (N=14)			
	Male	9(64.28%)	395.85	218.85
	Female	5(35.71%)	320.26	198.20
3	Location : (N=13)			
	Head of pancreas	11(84.6%)	445.08	253.6
	Body and tail	2(15.38%)	173.18	193.8
4	Tumor size : (N=13)			
	<4CMS	6(46.15%)	211.30	182.3
	>4CMS	7(53.84%)	548.35	306.7
5	Neoplasm : (N=13)			
	Benign	01(14.28%)	62.35	62
	Malignant	12(85.71%)	420.35	252.25

Out of 9 cases studied in gall bladder tumors, 2 cases of choledocholithiasis were considered and the rest 7 cases were of gall bladder carcinoma/ cholangiocarcinoma.

RELATIONSHIP BETWEEN CLINOPATHOLOGICAL FACTORS AND CA 19-9 VALUES IN GALL BLADDER TUMORS AND CHOLEDOCHOLITHIASIS :

SR. NO.	CLINOPATHOLOGICAL FACTORS	NUMBER	CA 19-9 (MEAN)	CA 19-9 (MEDIAN)
1	Age : (N=9)			
	20 – 39 yrs	0	00	00
	40-59 yrs	5(55.55%)	161.27	86.6
	> 60 yrs	4(44.44%)	301.225	213.05
2	Sex: (N=9)			
	Male	6(66.6%)	316.45	40
	Female	3(33.3%)	166.32	120
3	Neoplasm : (N=9)			
	Benign	2(16.66%)	28.66	23
	Malignant	7(77.7%)	254.43	123.8

Out of 6 cases of periampullary carcinoma studied, there were 2 cases of periampullary adenoma and 4 cases of periampullary carcinoma.

RELATIONSHIP BETWEEN CLINOPATHOLOGICAL FACTORS AND CA 19-9 VALUES IN PERIAMPULLARY TUMORS

SR. NO.	CLINOPATHOLOGICAL FACTORS	NUMBER	CA 19-9 (MEAN)	CA 19-9 (MEDIAN)
1	Age : (N=6)			
	20 – 39 yrs	1(16.5%)	88	88
	40-59 yrs	3(50%)	210.88	35
	> 60 yrs	2(33.5%)	251.36	300
2	Sex: (N=6)			
	Male	4(53.84%)	230.43	180
	Female	2(33.5%)	186.633	158.4
3	Neoplasm : (N=6)			
	Benign	1(16.5%)	48.26	36.8
	Malignant	5(83.5%)	258.80	290

STATISTICAL ANALYSIS OF CA 19-9(WHEN CUT OF IS 37U/ML) : For Pancreatic Carcinoma sensitivity is 87.5% , Specificity is 90%, Positive Predictive Value(PPV) is 91.3% and Negative Predictive Value(NPV) is 40%. For Cholangiocarcinoma sensitivity is 80% , Specificity is 66.6%, Positive Predictive Value(PPV) is 92.3% and Negative Predictive Value(NPV) is 40%.For Periampullary Carcinoma sensitivity is 70% , Specificity is 86.6%, Positive Predictive Value(PPV) is 87.5% and Negative Predictive Value(NPV) is 40%.

CONCLUSION

CA 19-9 values in normal individual is < 37 U/ml. Values >37 U/ml are considered abnormal. Higher pre-operative serum CA 19-9 value is associated with poor survival rate of patient. Less than 50% change in serum CA 19-9 level after therapy is also associated with poor survival rate. CA 19-9 is a reliable prognostic predictor for monitoring disease progression. Decrease in CA 19-9 value after surgery, radiotherapy of chemotherapy correlates with efficacy of treatment. Pre and post

operative CA 19-9 values are important to study. Post operative CA 19-9 value has definitive prognostic value to detect any metastasis or recurrence after successful surgery or chemotherapy. Therefore it can be concluded that CA 19-9 is an important tumor marker with sensitivity of 76.312% and specificity of 73.33% for gastrointestinal carcinoma. It should be used in conjunction with clinical features, radiological findings and fine needle aspiration to arrive at a diagnosis. Thus it is a useful supportive investigation in gastrointestinal carcinoma's.

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