Journal Homepage: -www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/15327
DOI URL: http://dx.doi.org/10.21474/IJAR01/15327

RESEARCH ARTICLE

ROLE OF CARBOHYDRATE ANTIGEN (CA19-9) AND CARCINOEMBRYONIC ANTIGEN (CEA) AS A PROGNOSTIC FACTORS IN PANCREATIC CARCINOMA

Jamshed Alam[1], Muhib Ullah[2], Muhammad Usman[3], Imran Ud Din Khan[4] and Iltaf Hussain[5]

1. Associate Professor, Department of General Surgery, Hayatabad Medical Complex, Peshawar, Pakistan.
2. SPR, Surgical A Unit, Department of General Surgery, Hayatabad Medical Complex, Peshawar, Pakistan.
3. SPR, Surgical B Unit, Department of General Surgery, Hayatabad Medical Complex, Peshawar, Pakistan.
4. SPR, Surgical C Unit, Department of General Surgery, Hayatabad Medical Complex, Peshawar, Pakistan.
5. Health Science Center, Xi'an Jiaotong University, Shaanxi, China.

Manuscript Info

Manuscript History
Received: 05 July 2022
Final Accepted: 09 August 2022
Published: September 2022

Keywords:-
CA19-9,Carcinoembryonicantigen, Pancreascarcinoma, Prognosis

Abstract

Objective: To investigate the potential utility of pre-treatment carcinoembryonic antigen (CEA) and carbohydrate antigen (CA 19-9) as prognostic indicators to assess prognosis in pancreatic carcinoma.

Materials and Methods: This retrospective observational study was carried out at the Department of General Surgery Hayatabad Medical Complex Peshawar from July 2017 to June 2022. A total of 70 patients with the diagnosis of pancreaticcarcinoma were enrolled. All patients were histologically diagnosed with pancreatic carcinoma. The levels of CA19-9 and CEA were evaluated before treatment.All patients received either an operation, chemotherapy or chemoradiotherapy (CRT), and patients who only received supportive care, palliative surgery or other treatments were not included in the study. Patients with a history of other malignancies were excluded.

Results:A total of 70 patients were included in this study. Age ranged between 25-75 years, with a mean age of 50 years. Included patients were stratified into 2 groups (35 each) in regard to their preoperative CEA & CA 19-9 level. Group 1: (Normal serum level group, CEA level value <5ng/ml & CA19-9 <37 U/ml), Group 2: (Elevated level group ≥5ng/ml & ≥37 U/ml)There were 19(54.3%) males and 16(45.7%) females in group 1 with male to female ratio of 1.18:1 and 18(51.4%) male & 17(48.6%) females in group 2 with male to female ratio 1.05:1. CA 19-9 and CEA were evaluated at initial diagnosis, and the median levels were 37U/mL (range,0.1-20000U/mL) and 3.4 ng/mL (range, 0.04-8566 ng/mL), respectively.

Conclusion: Patients with elevated serum CEA levels at diagnosis demonstrated poor overall survival. Pre-treatment CEA level may predict the prognosis of patients with pancreatic adenocarcinoma.

Corresponding Author:- Muhib Ullah
Address**:-** SPR, Surgical A Unit, Department of General Surgery, Hayatabad Medical Complex, Peshawar, Pakistan.

Introduction:-

Pancreatic cancer is one of the most deadly cancers and the fourth-leading cause of cancer-related death worldwide(Dong, Jia et al. 2018). The only curative method of treating pancreatic cancer is surgical resection. However, only 5-25% of pancreatic cancer patients qualify for curative pancreatectomy(De Rosa, Cameron et al. 2016). With other treatment approaches, the overall 5-year survival is less than 5% for these patients, most of whom are inoperable at diagnosis (Distler, Pilarsky et al. 2013). Survival of pancreatic cancer patients has remained similar since the development of Whipple's procedure and gemcitabine. To provide more effective treatment to these patients, studies have set out to find biomarkers for better diagnosis and prognosis.

Prognostic factors can predict treatment response and assess the risk of disease progression. In the future, these markers may be able to guide personalized therapy. So far, several tumor markers of pancreatic cancerhave been reported. Among them, carbohydrate antigen (CA)19-9 is the standard tumor marker for pancreatic cancer. CA 19-9 has proven helpful in differentiating benign from malignant pancreatic diseases. The sensitivity of CA 19-9 ranges from 41 to 86%, with a specificity of 33 to100%(Edge and Compton 2010). Carcino-embryonicantigen (CEA) is the most commonly used tumor marker for gastrointestinal malignancies. It was initially developed for pancreatic cancer and was used throughout 1970-1980 before the advance of CA19-9. Currently, CEA is the standard tumor marker for screening and predicting the prognosis of colorectal cancer (Fujioka, Misawa et al. 2007).

Preoperative CA19-9 levels might predict pancreatic cancer's resectability. Additionally, it has been demonstrated that the pre-treatment CA19-9 level affects how well pancreatic cancer patients respond to chemotherapy or chemoradiotherapy(Goonetilleke and Siriwardena 2007, Grunnet and Sorensen 2012). However, less is known regarding the relationship between pre-treatment CEA level and pancreatic cancer prognosis. CEA might also be helpful in predicting pancreatic cancer, considering its background and usefulness in gastrointestinal malignancies. The capability of CA 19-9 and CEA to serve as prognostic indicators has not yet been explored(Gulley, Madan et al. 2011, Siegel, Ward et al. 2011).

To determine the effectiveness of pre-treatment CA19-9 and CEA in predicting the prognosis of patients with pancreatic carcinoma, we included patients with pancreatic cancer in this study, regardless of stages and possible treatments, and analyzed the factors associated with survival.

Material And Methods:-

This retrospective observational study was carried out at the Department of General Surgery Hayatabad Medical Complex Peshawar from July 2017 to June 2022. A total of 70 patients with the diagnosis of pancreaticcarcinoma was enrolled. All patients were histologically diagnosed with pancreatic carcinoma. The levels of CA19-9 and CEA were evaluated before treatment. All patients received either an operation, chemotherapy, or chemoradiotherapy (CRT), and patients who only received supportive care, palliative surgery, or other treatments were not included in the study. Patients with a history of other malignancies were excluded. Clinical variables used in this study were sex, age, hypertension, diabetes mellitus, Eastern Cooperative Oncology Group (ECOG), stage, tumor location, tumor size, albumin, total bilirubin, CA 19-9 level, CEA level, and treatment modality.The standard diagnostic cut-off values for CA19-9 and CEA were used 37U/mL and 5ng/mL, respectively. All tumors were classified as resectable pancreatic cancer (stage I and II), locally advanced pancreatic cancer (stage III), and advanced pancreatic cancer (stage IV) using the TNM staging system. The Institutional Review Board approved this study for human research. The correlations of CA 19-9 level and CEA level with tumor stages were evaluated using Spearman correlation.The Kaplan-Meier methods estimated survival in different subgroups.

Statistical analysis was performed using SPSS software version 23.0. Microsoft Excel 2013 was used for tables and graphs. A p-value of ≤ 0.05 was considered statisticallysignificant.

Results:-

A total of 70 patients were included in this study. Age ranged from 25 to 75 years, with a mean age of 50 years. Patients were stratified into 2 groups (35 each) regarding their preoperative CEA & CA 19-9 levels. Group 1: (Normal serum level group, CEA level value <5ng/ml & CA19-9<37 U/ml), Group 2: (Elevated level group ≥5ng/ml& ≥37 U/ml)

There were 19(54.3%) males and 16(45.7%) females in group 1 with male to female ratio of 1.18:1 and 18(51.4%) male &17(48.6%) females in group 2 with male to female ratio 1.05:1.

CA 19-9 and CEA were evaluated at initial diagnosis, and the median levels were 37U/mL (range, 0.1-20000U/mL) and 3.4 ng/mL (range, 0.04-8566 ng/mL), respectively.

CA 19-9 was increased above 37 U/mL in 29(82.8%) patients and CEA above 5ng/mL in 24(68.6%) patients accordingly.**Fig-I**

Tumor localization in group 1 were: 19(54.3%) tumors in the head of the pancreas, 11(31.4%) in the tail of the pancreas and 5(14.3%) at the body of pancreas respectively.In group2: 21(60%) tumors were found in the head,10(28.6%) in the tail,and 4(11.4%) in the body of the pancreas,respectively (P=0.702). The initial ECOG score in group 1 was, 0 in 22(62.9%) and 1-2 in 13(37.1%), while in group 2 this score was 0 in 17(48.6%) and 1-2 in 18(51.4%) respectively (P=0.005). Tumor size in group 2 was (3.7±1.3 cm) as compared to group1 (3.0±0.8 cm) P=0.005.The mortality rate was43(61.4%) at the time of the final analysis. The median overall survival of group1 was 18.5 months (range, 15.2-21.8 months) months and group2 were 12 months (Range 8.3-15.7 months) respectively (P=0.001). Table-1

The association between survival and the parameters of sex, age, ECOG, location of tumor, size of tumor, level of CEA& CA19-9 were analyzed by univariate analysis, which showed that ECOG (1 and 2), tumor stage, location & size of tumor (>3 cm) and elevated serum levels of CEA& CA19-9 (>5 ng/mL& ≥37 m/Ul) were significantly associated with poor overall survival.

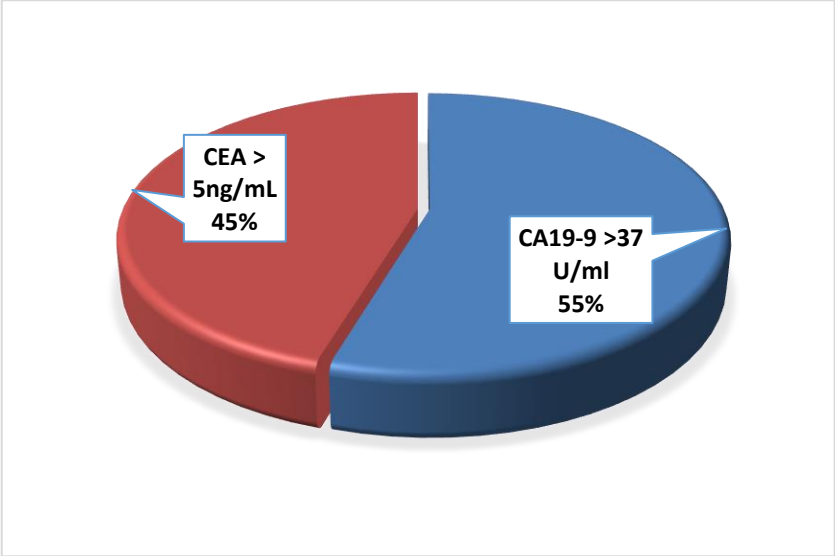

Figure I:- Elevated Level Frequency.

Table1:- Outcome Of Both Groups.

Outcome	**Group 1**		**Group 2**		P value
	Frequency	Percentage	Frequency	Percentage	
GENDER					
Male	19	54.3%	18	51.4%	0.801
Female	16	45.7%	17	48.6%	
TUMOUR LOCATION					
Head	19	54.3%	21	60%	0.702
Tail	11	31.4%	10	28.6%	
Body	5	14.3%	4	11.4%	
ECOG Score					
0	22	62.9%	17	48.6%	0.005

1-2	13	37.1%	18	51.4%	
TUMOR SIZE					
Tumor size	3.0±0.8		3.7±1.3cm		0.005
SURVIVAL RATE					
Median survival	18.5		12		0.001
MORTALITY					
Overall mortality	43	61.4%	43	61.4%	------

Discussion:-

Pancreatic carcinoma is an aggressive tumor with a dismal outlook is pancreatic carcinoma. Additionally, pancreatic cancer patients frequently find metastatic disease or an inoperable condition. Not all patients respond well to standard anti-cancer treatment, although treatment plans are created based on the tumor's stage, the patient's health, and a number of other clinical criteria. Studies have examined the effectiveness of several tumor markers for better treatment response prediction, cancer progression risk, and medical expense prediction in pancreatic cancer(Kim, Kim et al. 2009, Bünger, Laubert et al. 2011). CA 19-9 and CEA are the most frequently used tumor markers for pancreatic cancer. The most often utilized biomarker for pancreatic cancer is CA 19-9, which was initially derived from a colorectal cell line (Hess, Glimelius et al. 2008). Although CA19-9 is not suitable as a screening marker in asymptomatic patients, it is useful for differentiating benign disease from a malignant pancreatic disease. Also, a few studies reported that preoperative CA19-9 was correlated with resectability and prognosis after surgery (Halloran, Ghaneh et al. 2008, Koom, Seong et al. 2009). In addition, postoperative CA19-9 can predict overall survival and disease-free survival after pancreatic cancer resection and adjuvant chemotherapy (Koom, Seong et al. 2009). Since its discovery more than 45 years ago, CEA has mostly been used to track colorectal cancer. Although CEA has been used to treat pancreatic cancer, its sensitivity and specificity are insufficient to serve as a biomarker for diagnosis. Instead, the resectability of pancreatic cancer has been predicted using a preoperative combination of CEA and CA 19-9 (Mehta, Prabhu et al. 2010). Additionally, a few studies claimed that pre-treatment CEA was linked to unsatisfactory treatment outcomes (Berger, Garcia Jr et al. 2008, Goonetilleke and Siriwardena 2007, Molina, Augé et al. 2010). However, these studies used a wide range of cut-off values, a small number of patients, a certain tumour stage, or a particular treatment method to determine whether CA19-9 and CEA can be generally applicable prognostic markers of pancreatic cancer, the use of these biomarkers should be tested in a large number of patients with various stages of pancreatic cancer (Kaufman, Lenz et al. 2008).

In this study, we analyzed 70 patients diagnosed with pancreatic carcinoma. Cancers of stages1to 4 according to AJCC staging were all included, and the standard diagnostic cut-off values of CA19-9 and CEA were used. All patients received either an operation, chemotherapy, or CRT. In the elevated CEA level group, tumor size was more significant than the normal CEA level group, and CEA level showed a positive correlation with tumor stages. In addition, our results showed that pre-treatment CEA level was significantly associated with overall survival regardless of stages. In the unresectable group, the normal serum CEA level group showed longer progression-free survival than the elevated serum CEA level group. However, the elevated CA19-9 was not significantly associated with poor overall survival and progression-free survival.There might be several reasons for this result. First, patients with Lewis blood typenegative do not express the CA 19-9 antigen and inflammatory lesions of the pancreas can increase CA 19-9 level, even in low stages. Also, obstructive jaundice might increase the level of CA 19-9, which is an important source of false positive results (Long, Van Dam et al. 2005).

Although there is a well-established link between CEA and colon cancer, it has also been found to be a prognostic marker in a number of other malignancies, including breast cancer, cervix cancer, and lung cancer(Halloran, Ghaneh et al. 2008). In our study, CEA showed promise as a prognostic indicator for pancreatic cancer, particularly in patients who underwent non-surgical treatment. We were unable to demonstrate the value of CEA in the surgically treated group because of a limited number of patients with increased CEA had operable malignancy. In the non-surgical group, CEA was linked to progression-free survival rather than the treatment response. This shows that chemo-resistance was acquired earlier and that there may have been different cancer behaviors. Several more research revealed a connection between CEA and the ability of metastasis. The cell surface expresses CEA, which aids in cellular adhesion (Petrushnko, Gundara et al. 2016). As a result, cancerous cells may become worse and spread through increased CEA expression. With the recent development of numerous cancer vaccines that target CEA, therapy outcomes for pancreatic cancer patients with increased CEA may be improved. This makes pancreatic cancer an excellent target for cancer vaccinations(Petrushnko, Gundara et al. 2016).

Conclusion:-

Significant prognostic information on patients with pancreatic cancer was provided by pre-treatment increased CEA levels using the usual diagnostic cut-offvalue. To determine whether CEA has predictive value for treatment modalities and chemotherapy regimens, more research is required. In addition to CA 19-9 and CEA, additional research must be conducted on and comparisons made with other possible biomarkers that might be helpful for screening, diagnosing, and predicting treatment outcomes.

Acknowledgement:-

The authors are thankful to the patients for their cooperation.

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