

Clinical Significance of CA125 Level with Clinicopathological Variables and Peritoneal Dissemination in Patients with Gastric Carcinoma

Abstract

Background: Serum tumor markers have been shown to correlate with the clinical status of patients with advanced gastric cancer. However, the clinical significance of tumor marker in patients with peritoneal dissemination has not been fully verified. Peritoneal metastasis is a crucial factor for the prognosis in gastric cancer, but its diagnosis is difficult before laparotomy. This study analyzed the usefulness of tumor marker CA125 level in gastric cancer & diagnosis of peritoneal metastasis in gastric cancer.

Objective: This study is an evaluation of serum levels in the tumor markers CA125 in gastric cancer patients in preoperative periods to determine the Relationship of preoperative CA125 level with clinicopathological variables & to predict association of CA125 level with peritoneal dissemination in gastric carcinoma.

Methods: A prospective cross sectional study was done of 61 patients diagnosed with gastric cancer treated at a single institution in Bangladesh National Institute of Cancer Research and Hospital, Mohakhali, Dhaka, Bangladesh from July 2010 - December 2011. Analyses were performed to identify patient and tumor-related characteristics and to identify peritoneal metastasis. The sera from 61 patients with gastric cancer were measured for CA125 levels using a commercial immunoradiometric assay. All the patients underwent diagnostic imaging with computed tomography (CT) or ultrasound (US) before laparotomy. Peritoneal involvement was confirmed by either ascites diagnosed by USG or CT, direct visualization of metastatic deposits during surgery and detection of cancer cell by peritoneal wash fluid taken after laparotomy.

Results: The serum levels of CA125 the cutoff value of 35 U/ml was regarded as positive. Preoperative levels of CA125 were above the cut-off levels in 23% of all cases. A total of 30(49.2%) patients were showed peritoneal involvement. The CA125 level was significantly correlated with the degree of peritoneal dissemination and the existence of malignant ascites. In particular, the serum CA125 levels showed sensitivity 73%, specificity 86%, and the highest odd ratio (18.33 95% CI) for predicting peritoneal metastasis. The positive and negative predictive values of CA125 were 65% and 91%, respectively. So in this study preoperative serum CA125 levels may provide a value in determining depth of invasion, lymph node involvement & metastasis in patients with gastric cancer. CA125 was very sensitive in detecting peritoneal dissemination in gastric carcinoma patients.

Conclusion: In this study Preoperative serum Measurement of the serum CA125 titer may be a powerful predictor of peritoneal metastases in patients with gastric carcinoma & may provide a value in determining depth of invasion, lymph node involvement & metastasis in patients with gastric cancer.

Keywords: CA125 level; Peritoneal metastasis; Gastric carcinoma

Research Article

Volume 4 Issue 2 - 2016

Laila Shirin* and Md Mizanur Rahman

Department of surgical oncology, National Institute of Cancer Research and Hospital Mohakhali, Bangladesh

*Corresponding author: Laila Shirin, Assistant professor, Department of surgical oncology, National Institute of Cancer Research and Hospital Mohakhali, Dhaka, Bangladesh, Email: dr.lshirin@gmail.com

Received: October 23, 2015 | Published: February 10, 2016

Introduction

Serum CA125 levels are known to be elevated in peritoneal inflammation and in carcinomatosis, and are widely used in the diagnosis of ovarian cancer [1]. A significant relationship between CA125 and gastric cancer with peritoneal dissemination has also been reported [2].

Recently, various tumors markers have been developed and

it is known that the serum levels of markers such as carcino-embryonic antigen (CEA), carbohydrate antigen 19-9 (CA 19-9) and carbohydrate antigen 125 (CA125) are elevated in patients with advanced gastric cancer [3]. However, the clinical usefulness of tumor markers has not been well defined from a diagnostic and therapeutic point of view. Tumor markers are not useful in diagnosis or screening disease because of low sensitivity and specificity. Reports have shown the value of tumor markers as a prognostic factor for patients with advanced gastric cancer [4].

Distribution of carbohydrate antigen 125 (CA125) in mesothelial cells of the peritoneum, pleura, and pericardium, as well as in the epithelium of the fallopian tubes, endometrium and endocervix which suggests that dissemination of gastric carcinoma to the peritoneum may affect the serum levels of CA125 [2]. Although not produced by gastric Cancer cells and with no relation to the histological Subtypes, CA 125 is usually elevated in serum when the disease has invaded the serous membrane and the peritoneal cavity [5]. Although prognosis is mainly determined by tumor stage at the time of gastric cancer surgery, recent studies have assessed the usefulness of preoperative tumor marker levels to predict invasiveness and prognosis [6].

Nevertheless, current serum tumor markers are primarily used for the preoperative staging of neoplasms, postoperative monitoring of treatment effectiveness, and early diagnosis of recurrence, as they can be easily and cost-effectively identified [7].

Peritoneal metastasis is a crucial factor for the prognosis in gastric cancer, but its diagnosis is difficult before laparotomy. Diagnosis for the disease currently involves recognition of ascites on physical examination, recognition of induration of the pouch of Douglas by digital examination, or the use of abdominal computed tomography (CT) or ultrasonography (US). However, none of these methods has demonstrated a high predictive value [8]. Therefore until now, laparotomy plays an important role in the diagnosis of peritoneal metastasis by the direct observation of peritoneal cavity.

Peritoneal cytological washing is the gold standard for determining peritoneal spread of gastric carcinoma, yet its sensitivity is relatively low, lying in the 14% to 21% range for gastric carcinoma with serosal invasion [9]. Preoperative serum CA125 levels may provide a predictive value in determining peritoneal metastasis in gastric cancer. Therefore this study analyzed the usefulness of tumor marker with clinicopathological parameters and peritoneal metastasis in gastric cancer.

Methodology

Aims and objective

To determine the Relationship of preoperative CA125 level with clinicopathological variables & to predict association of CA125 level with peritoneal dissemination in gastric carcinoma. Inclusion criteria for the study was histologically diagnosed cases of gastric adenocarcinoma and exclusion criteria were patients already received operative treatment, chemotherapy and radiotherapy, patients who have no CA125 level and who do not want to include in the study.

Patient evaluation

Selected patients with adenocarcinoma of the stomach diagnosed by endoscopy of upper GIT with biopsy were evaluated for treatment. Among investigations Ultrasonogram of whole abdomen, Barrium meal of stomach, CT scan of abdomen, Serum CA125 level. Peritoneal fluid or Ascites fluid were also taken for cytology in all patients.

Collection of blood sample

Peripheral blood samples for CA125 were obtained from each patient before surgery. Their data were used for comparison with the patients clinicopathological parameters & with the patients in whom peritoneal carcinomatosis was present in carcinoma stomach.

Specimen collection

The presence of peritoneal metastasis was diagnosed though one of the following means USG/computed tomography, a positive cytology after peritoneal aspiration or lavage, or direct visualization through open surgery. Peritoneal washing for cytologic examination was performed immediately after the laparotomy or ascitic fluid before and in some cases after laparotomy.

Assay: The sera were assayed for CA125 with an immunoradiometric assay using a Pathozyme ovarian cancer antigen (OD287), Omega Diagnostics Ltd. UK.

Intraoperative staging: At operation, gastric cancers were staged for local, nodal and metastatic spread.

Results

From July 2010-December 2011, sixty one patients diagnosed as adenocarcinoma of stomach was undertaken for study from National Institute of Cancer Research and Hospital, Mohakhali, Dhaka, Bangladesh. The patients' clinicopathological factors are shown in Table 1. In the study 37 patients' age was <55 years (60.7%) and 24 patients' age was >55 years (37.3%). The mean age of the patients was 52.89 years (\pm SD, 12.11 years; range, 20-80 years). Three fourth of the patients was male (46, 75.4%) with a male female ratio of 3:1. A total of 17 (27.9%) patients were positive for serum 125 (range = 0.80 -1747.80 ng/mL).

The patients' sex distribution were shown in Figure 1. In the study 46 patients was male (75%) and 15 patients was female (25%) with a male female ratio of 3:1. Among the patients histogram (Figure 2) showed that most of the patients age was more than 45 years.(19 patients' age was 45-54 years, 17 patients was 55-64 years and 12 patients was >65 years) at the time of presentation.

Table 2 showed Demography of the patients with gastric cancer in 61 cases. Symptoms at presentation, were weight loss in 41.0% , vomiting in 67.2%. Pain on epigastrium was presented by 63.9%, anorexia by 55.7%, of patients. Malena was presented in 13.1%. Regarding haemoglobin level in 55.7% cases had 7-10 gm/dl. Nutritional Status poor in 37.7%, average in 47.5% cases. Anemia requiring transfusion in 39.3%. History of smoking in this group was 60.7%. Primary tumor site was the pyloric part 42.6%, body and antrum in 19.7% & diffuse involvement of stomach in 36.1 % patients.

Table 3 showed that most of the patients were at stage III (29.5%) and at stage IV (50.8%). Among differentiation moderately differentiated 45.9% & poorly differentiated was 39.3%. Distal gastrectomy was performed in 45.9% and gastric bypass surgery in 14.8% patients.

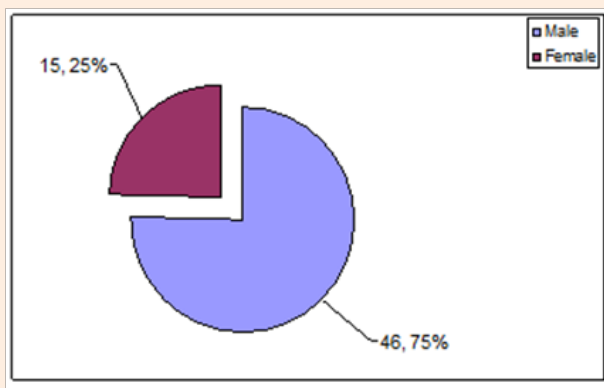


Figure 1: Sex distribution of the patients.

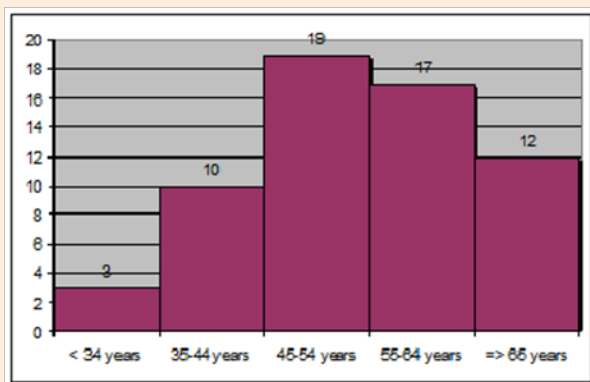


Figure 2: Histogram showing age distribution of the patients.

Table 4 a total of 49.2% patients were showed peritoneal involvement. Peritoneal involvement was confirmed by either ascites diagnosed by USG or CT, direct visualization of metastatic deposits during surgery and detection of cancer cell by peritoneal wash fluid taken after laparotomy. Ascites was present in 24.6% patients. Ascites was diagnosed by USG or CT in 16.4% and after laparotomy 8.2%) cases. Ten patients (16.4%) were diagnosed with peritoneal disseminations metastatic deposits during surgery. Free cancer cells were detected in 5 patients (8.2%).

In Table 5 clinico-pathological factors was compared with patients positive and negative for Serum CA 125. There was no correlation with CA125 and age (P.32), sex (P. 09) & with depth of invasion (P.25). There was significant correlation with the histologic type and CA125 positivity (P .01), Lymph node metastasis (P.03). The CA125 level was significantly associated with the peritoneal involvement (P<.001). Significant difference was not observed for CA125 (P 0.2) with early and advanced stages of gastric carcinoma confirmed after surgery.

Table 6 shows a comparison of tumor marker for peritoneal dissemination. For CA125 cutoff value ≥ 35 U/ml was used as a reference value for peritoneal dissemination. However, CA125 had a very high odds ratio of 18.33 for predicting peritoneal dissemination among the markers tested. CA 125 level was more significantly associated with the peritoneal involvement (P<.001).

The sensitivity and specificity of CA125 were found to be 73% and 86% and the positive and negative predictive values of CA125 were 65% and 91%, respectively Table 7.

Table 1: Patient Characteristics (n=61).

Variable	Number	%
Age		
<55	37	60.7
>55	24	39.3
Sex		
Male	46	75.4
Female	15	24.6
CA125 level		
35IU/L	44	72.1
>35IU/L	17	27.9

CA 125 (Cancer antigen! 25)

Table 2: Demography of the patients with gastric cancer (n=61).

Variable	Value	%
Symptoms at Presentation		
Weight loss	25	41
Vomiting	41	67.2
Pain on epigastrium	39	63.9
Anorexia	34	55.7
Dysphagia	4	6.8
Malena	8	13.1
Lump on abdomen	18	21.3
Haemoglobin Level		
5-7 gm/dl	4	6.6
7-10 gm/dl	30	55.7
> 10 gm/dl	23	37.7
Nutritional Status		
Poor	23	37.7
Average	29	47.5
Good	9	14.8
Anemia requiring Transfusion	24	39.3
History of Smoking	37	60.7
History of Alcohol use	2	3.3
Primary Tumor Site		
Pyloric part	26	42.6
Body and antrum	12	19.7
Fundus & GO junction	1	1.6
Diffuse involvement	22	36.1

Table 3: Pathological characteristics and operability of the patients in gastric cancer (n=61).

Variable	Number	%
Stage		
I	4	6.6
II	8	13.1
III	18	29.5
IV	31	50.8
Resectability		
Resectable	33	54.1
Non resectable	18	29.5
Not operated	10	16.4
Grading		
Well differentiated	9	14.8
Moderately differentiated	28	45.9
Poorly differentiated	24	39.3
Type of Operation		
Distal radical gastrectomy (D1)	24	39.3
Palliative distal radical gastrectomy	4	6.6
Total radical gastrectomy	5	8.2
Palliative gastrojejunostomy	9	14.8
Feeding jejunostomy	8	13.1
No operation	11	18

Table 4: Characteristics of peritoneal dissemination.

Peritoneal Dissemination	Number	%
Peritoneal cytology +ve	5	8.2
Visible seedling on OT	10	16.4
Ascites on USG or CT	10	16.4
Ascites on OT	5	8.2
Peritoneal cytology -ve	31	50.8

Table 5: Comparison of Clinico-pathological Factors in Patients.

Factor	CA 125 + ve		CA 125 - ve		p value
	n	%	n	%	
Sex					
Male	10	58.8	36	81.8	0.09
Female	7	41.2	8	18.2	
Age					
≤ 55	12	32.4	5	20.8	0.32
> 55	25	67.6	19	79.2	
Histological Type					
Differentiated	6	35.3	31	70.5	0.013
Undifferentiated	11	64.7	13	29.5	
Depth of Invasion					
Upto Serosa (T1+T2+T3)	4	36.4	27	65.8	0.078
Beyond Serosa(T4)	7	63.6	14	34.2	
Lymph Node Metastasis					
Perigastric (N0+N1)	3	27.3	29	70.8	0.012
Beyond (N2+N3)	8	72.8	12	29.3	
Peritoneal Involvement					
Negative	3	17.6	28	63.6	<.001
Positive	14	82.4	16	36.4	
Stage					
Early stage	1	5.8	11	50	0.2*
Advanced stage	16	94.2	11	50	

Chi- square test is done to detect significance

*Fissure Exact test was done to detect significance

Positive and Negative for Serum CA 125.

Table 6: Comparison of the Diagnostic Ability of Serum Tumour Marker.

Tumour Marker		Peritoneal Dissemination		Odds Ratio	95% CI	χ ² test	P value
		Positive	Negative				
		(no. of patients)	(no. of patients)				
CA 125	Positive ^a	11	6	18.33	4.39-76.64	20.45	<.001
	Negative ^b	4	40				

Level for Peritoneal Dissemination

95% CI: 95% confidence interval.

^aPositive indicates the serum levels of CA 125 was ≥ the cutoff value of 35 U/ml.

^bNegative indicates the serum levels of CA 125 was ≤ the cutoff value of 35 U/ml

Table 7: Sensitivity, Specificity positive and negative predictive value of the Tumour markers. 95% CI: 95% confidence interval.

Tumor Marker	Sensitivity	Specificity	Predictive Value Positive	Predictive value Negative (95% CI)
	(95% CI)	(95% CI)	(95% CI)	
CA 125	73%(44-91)	86% (73-94)	65% (39-85)	91% (77-97)

Discussion

Despite progress in recent years towards the early detection of gastric cancer in the western country and Japan, most patients will already have advanced disease at diagnosis in our country. The majority of patients will die of recurrent disease, even if surgery is thought to be curative at the time.

Recent advances in preoperative diagnosis using ultrasonography or computed tomography provide much more information on peritoneal metastasis before operation. However, it is impossible to obtain information about small peritoneal metastasis preoperatively. Therefore, PWC must be performed in addition to macroscopic observation and palpation in patients with advanced gastric cancer. Therefore, cases positive for PWC are considered as peritoneal metastasis, according to the JCGC [10,11].

The prognostic value of positive cytology findings was recently confirmed also in the West, and a new stage classification for gastric carcinoma, recently published by Japanese Gastric Cancer Association, employs the result of cytologic examination (Cy categories) as one of the key prognostic factors [12].

Gastric cancer-specific tumor markers have not yet been identified, and the tumor markers currently in use have very little benefit as screening tests due to their low sensitivity in early gastric cancer. Although CEA and CA 19-9 are not applied to TNM staging according to the American Joint Committee on Cancer (AJCC) 7th edition [13], they have been recognized as prognostic factors [14].

Although not produced by gastric Cancer cells and with no relation to the histological Subtypes, CA125 is usually elevated in serum when the disease has invaded the serous membrane and

the peritoneal cavity [5]. Present study based on Relationship of preoperative CA125 level with clinicopathological parameters & the prediction of peritoneal dissemination in patients with carcinoma stomach by detection of peritoneal involvement and compare with the level of preoperative serum CA125 level.

In the study mean age of the patients was 52.89 years (SD, 12.11 years; range, 20-80years). Male & female ratio was 3/1. The mean age of the patients was 52.89 years (SD, 12.11 years; range, 20-80years). Similar to our study the mean age of the patients with gastric carcinoma were 59 years & 58 years [15,16]. But in other studies mean age was 63.6 ± 11.7 years [9], the mean age of the patient was 61.4 years [12].

In general, men are more affected by the disease than women and, as with most solid organ malignancies, the incidence increases with age [17]. In this study number of male 46 (75.4%) female 15 (24.6%) ratio was 3/1. Similar Result was found in another study in bangladesh for gastric adenocarcinoma in which male and female ratio was 2.36:1 [18]. In different series, this has been reported as 29 (63.0%) were males and 17 (37.0%) females by Filho RC et al. [9], Ucar E et al. [16] the male/female ratio was 1.9/1 and according to Kodera Y et al. [12] male-to-female ratio of 3:2.

Serum CA125 level was measured preoperatively in patients with gastric cancer. A total of 17 (27.9%) patients were positive for serum 125. Nakata B [2] found that in the patients with gastric carcinoma, serum CA125 values had values above the cutoff value in 7.3 cases. According to Hwang GI [8], tumor markers, CA125 showed detection rates of peritoneal metastasis 38.6% cases. As the degree of peritoneal dissemination increased positive rate of CA125 increased. Preoperative serum CA125 level were elevated in 28(52.8%) cases in the study conducted by Bold RJ et al. [19].

Demography of the patients with gastric cancer in 61 cases showed on Table 2. Symptoms at presentation were weight loss in 25 (41.0%) Wt loss by Sougioultzis [20] was 28.9% & similar to our study. Vomiting was presented in 41(67.2%) but it was 75% of cases in study by SA Chowdhury [21]. Pain on epigastrium was presented by 39 (63.9%) but in Sougioultzis [20] Malena was presented in 8 (13.1%) in our study but by SA Chowdhury [21]. Hemetemesis and Melena presented by 6.94% cases Anemia requiring transfusion was in 24 (39.3%) in this study which was similar to Sougioultzis [20] where blood transfusion needed in 41.2% cases. History of smoking in this group was 37 (60.7%) Smoking was 57% cases by SA Chowdhury [21]. Primary tumor site was the pyloric part 26 (42.6%) body and antrum in 12 (19.7%) diffuse involvement of stomach in 22(36.1 %) patients. Similar involvement of antrum recorded by Sougioultzis [20] (42.4 %).

Those finding demarcate that most of our patients had tumors on pyloric part, most of them suffer from anaemia requiring blood transfusion. They had tendency of smoking but less alcohol intake. As most of the patients had tumors on pyloric part so vomiting was more presented by our patients than dysphagia.

The tumor staging was completed according to AJCC classification of gastric carcinoma. Most patients were at tumor at stage III (29.5%) and 31 at stage IV (50.8%). Most of the patients

were also in stage IV in many other studies also [16,22,23]. Among differentiation moderately differentiated 45.9% & poorly differentiated was 39.3%. In a study of our country. Most 57.12% of the gastric adenocarcinomas were poorly differentiated, 13.44% were moderately differentiated [18].

Distal radical gastrectomy was performed in 39.3% patients, palliative distal gastrectomy in 6.6%, similar result was found in other studies of our country. The maximum palliative surgery was distal partial gastrectomy [15]. But in our series gastric bypass surgery in 14.8% patients. In other series Gastrojejunostomy done in older group was 42% cases [21]. In other series by pass operation was done in 7.23% and 5% cases [18]. Among the resectable cases, distal gastrectomy in 45.9%, total gastrectomy 8.2% cases. Among the non resectable cases gastric bypass surgery in 14.8% patients. Fanelli F et al. [23] Forty percent of the patients underwent gastrectomy. Ucar E et al. [16], Total gastrectomy was performed in 58 patients, subtotal gastrectomy in 25, and gastric bypass surgery in 12. Study by Hayes N et al. [22] out of 85 patients thirteen cases were unsuitable for resection and simple bypass was performed in five of these, 11 cases with advanced disease had palliative resections. The tumor staging was completed according to AJCC classification of gastric carcinoma. Most patients were at tumor at stage III (29.5%) and 31 at stage IV (50.8%). Strikingly most of the patients in the study group was in advanced stage and a significant proportion was not suitable for operation. Most of the patients were also in stage IV in many other studies also [16,22,23].

The incidence of peritoneal cytology-positive cases seems to vary considerably among institutions. Total of 49.2% patients were showed peritoneal involvement in our study. It seems to be higher as we included noncuratively resected and also nonresectable cases in our study. The presence of peritoneal involvement was diagnosed though one of the following means: ultrasonography or computed tomography, a positive cytology after peritoneal aspiration or lavage, ascetic fluid aspiration or direct visualization through open surgery. Fanelli F et al. [23] also include same criteria for peritoneal metastasis.

Kodera Y et al. [12] in their study, cytology was positive in 21% patients. Hwang GI et al. [8] in his study revealed peritoneal dissemination in 15 of 88 patients. Study by Rosenberg R et al. [24] 21.4 per cent had detected free peritoneal cytology-positive in the peritoneal lavage. The cytological study of peritoneal washing conducted by Filho RC et al. [9] was positive in 15.2% patients.

In Table 5 clinico-pathological factors was compared with patients positive and negative for Serum CA 125. There was no correlation with CA125 and age (P.32) and sex (.09). There was significant correlation with the histologic type and CA125 positivity (P .01). But Emoto S [25] in their series, positive expression of CA125 did not correlate with the histological type of gastric cancer (p = 0.73).

There was correlation with Lymph node metastasis (P.03) and Stage (P.02). The CA125 level had no correlation with depth of invasion (P.25) in this study. Bold RJ [19] correlated both serum and peritoneal tumor markers where they found no association of the marker (CEA & CA125) and T & N stage except T4 lesions. But they determined marker level from peritoneal fluid only.

Study showed that although not produced by gastric Cancer cells and with no relation to the histological Subtypes, CA125 is usually elevated in serum when the disease has invaded the serous membrane and the peritoneal cavity [5]. CA125 level was significantly associated with the Peritoneal involvement ($P < .001$). The degree of peritoneal metastasis was also correlated with CA125 in study by [2,8,25].

The CA125 antigen has been observed in the peritoneum, particularly in areas of inflammation and adhesion. Peritoneal dissemination may cause inflammation of the peritoneum; therefore, one would expect that an elevation of serum CA125 would be observed in patients with peritoneal dissemination [2]. Emoto S [25] stated that the positivity of serum CA125 was significantly correlated with the presence of ascites. Their results also suggest that serum CA125 reflects the status of peritoneal lesions of gastric as well as ovarian cancer.

CA125 had the highest odds ratio 18.33(4.39-76.64) for predicting peritoneal dissemination among the markers tested (chi-square test). Similar to Hwang GI [8], where CA125 had also the highest odds ratio (24.46, 95% CI: 11.17-53.37). Nakata B [2] also proved that CA125 had the highest odds ratio for predicting peritoneal dissemination among the markers tested by chi-square test.

The sensitivity of CA125 was 73% (44%-91%), specificity 86% (73%-94%). So in this study CA125 was more sensitive in detecting peritoneal dissemination in gastric carcinoma patients. Similar result stated by Emoto S [25]. The sensitivities of CA125 were 46.1 Hwang GI [8]. CA125 had the best sensitivity 38.6% and best specificity 98.4% , diagnostic accuracy (91.5%) and Nakata B [2] the sensitivity of CA125 was 39.4% (13 of 33 patients) CA125 had the best specificity (95.7%).

Finding suggests that CA125 may have biological relevance in the progression or reduction of the peritoneal lesions of gastric cancer. Elevated CA125 may not simply be a result of disease progression, but may in fact have a causal relationship with the progression of peritoneal metastasis [25]. Emoto S [25] stated that serum CA125 and CA72-4 can now be considered valuable markers that reflect the quantitative volume of peritoneal dissemination in gastric cancer.

Finally extreme elevation of tumor marker in the setting of resectable gastric cancer should alert the oncologist of the high potential for recurrence & may warrant aggressive adjuvant therapy following curative gastrectomy [19].

Previous study showed that Adachi and colleagues [26] reported that in ovarian cancer, the serum CA125 level could be influenced not only by CA125 production by the primary tumor but also by CA125 production in the mesothelium. They suggested that an increase in serum CA125 level in the CA125-positive tumor group might reflect tumor progression; in the CA125-negative tumor group, this might reflect the development of ascites or peritonitis carcinomatosa. In fact, a previous study has shown that the production of CA125 by gastrointestinal tract cancer cells is infrequent [27]. Therefore, it may be more reasonable that an elevated level of CA125 is not derived from increased cancer cell volume but mainly reflects the severity of peritonitis caused by carcinomatosis.

Sensitivity of CA125 was 73% which was more than any other study. This might be due to the fact that advanced cases with ascites were also included in this study. This significance of increased sensitivity suggests that the serum levels of Serum CA125 is a clinically useful markers in diagnosis & would be highly suitable for monitoring peritoneal metastasis.

Conclusion

In this study Preoperative serum Measurement of the serum CA125 titer may be a powerful predictor of peritoneal metastases in patients with gastric carcinoma & may provide a value in determining depth of invasion, lymph node involvement & metastasis in patients with gastric cancer Like previous other studies we do not propose CA125 as a convenient marker for gastric cancer. But it may be useful in patients with high suspicious peritoneal metastasis prior to surgery. Therefore, surgeons can prevent unnecessary exploration and can be better prepared for available alternative therapy.

The limitations of this study include the relatively brief study period and the small sample size The use of diagnostic laparoscopy, which might allow more complete and reliable staging of recurrent abdominal disease, is rarely performed. Further research will be required to rectify these problems.

References

1. Rustin GJ, Vergote I, Eisenhauer E, Pujade Lauraine E, Quinn M, et al. (2011) Definitions for response and progression in ovarian cancer clinical trials incorporating RECIST 1.1 and CA 125 agreed by the Gynecological Cancer Intergroup (GCIIG). *Int J Gynecol Cancer* 21(2): 419-423.
2. Nakata B, Hirakawa YS, Chung K, Kato Y, Yamashita Y, et al. (1998) Serum CA 125 level as a predictor of peritoneal dissemination in patients with gastric cancer. *Cancer* 83(12): 2488-2492.
3. Sakamoto K, Haga Y, Yoshimura R, Egami H, Yokoyama Y, et al. (1987) Comparative effectiveness of the tumour diagnostics, CA 19-9, CA 125 and carcinoembryonic antigen in patients with diseases of the digestive system. *Cut* 28(3): 323-329.
4. Yamao T, Kai S, Kazemi A, Koizumi K, Handa T, et al. (1999) Tumor Markers CEA, CA19-9 and CA 125 in Monitoring of Response to Systemic Chemotherapy in Patients with Advanced Gastric Cancer. *Jpn J Clin Oncol* 29(11): 550-555.
5. Ohkura H (1999) Tumor Markers in Monitoring Response to Chemotherapy for Patients with Gastric Cancer. *Jpn J Clin Oncol* 29(11): 525-526.
6. Duraker N, Çelik AN (2001) The prognostic significance of preoperative serum CA 19.9 in patients with resectable gastric carcinoma: comparison with CEA. *J Surg Oncol* 76(4): 266-271.
7. Choi RA, Park JC, Kim JH, Shin SK, Lee SK, et al. (2013) High level of preoperative High level of preoperative carbohydrate antigen 19-9 is a poor survival predictor in gastric cancer carbohydrate antiAntigen CA 19-9 as a poor survival predictor in gastric cancer. *World J Gastroenterol* 19(32): 5302-5308.
8. Hwang GI, Yoo CH, Sohn BH, Shin JH, Park YL, et al. (2004) Predictive value of preoperative serum CEA, CA19-9 and CA125 levels for peritoneal metastasis in patients with gastric carcinoma. *Cancer Res Treat* 36(3): 178-181.

9. Filho RC, Palma RT, Giusti MF, Bueno Mde A, Silva PS, et al. (2008) Levels of carcinoembryonic antigen and CA 19-9 in the sera and peritoneal washing of patients undergoing surgical treatment for gastric carcinoma. *Arq Gastroenterol* 45(3): 219-224.
10. Japanese Gastric Cancer Association (1998) Japanese classification of gastric carcinoma - 2nd English edition. *Gastric Cancer* 1(1): 10-24.
11. Homma Y, Ushida S, Yamada M, Kobayashi H, Suzuki K (2010) Positive Peritoneal Washing Cytology in Multiple Cavities Can Predict Poor Prognosis of Advanced Gastric Cancer Patients. *Ann Surg Oncol* 17(2): 455-460.
12. Kodera Y, Yamamura Y, Shimizu Y, Torii A, Hirai T, et al. (1999) Peritoneal washing cytology: prognostic value of positive findings in patients with gastric carcinoma undergoing a potentially curative resection. *J Surg Oncol* 72(2): 60-65.
13. Edge SB, Byrd DR, Compton CC (2010) American Joint Committee on Cancer (AJCC) cancer staging manual. (7th edn), Springer publishing company, New York, USA, pp. 117-121.
14. Kim DH, Jong S, Cheong AH, Choi MG, Noh JH, et al. (2011) The Relationships Between Perioperative CEA, CA 19-9, and CA 72-4 and Recurrence in Gastric Cancer Patients After Curative Radical Gastrectomy. *J Surg Oncol* 104(6): 585-591.
15. Wobbes T, Thomas CMG, Segers MFG, Nagengast FM (1992) Evaluation of seven tumor markers (CA 50, CA 19-9 TruQuant, CA 19-9, CA 195, carcinoembryonic antigen, and tissue polypeptide antigen) in the pretreatment sera of patients with gastric carcinoma. *Cancer* 69(8): 2036-2041.
16. Ucar E, Semerci E, Ustun H, Yetim T, Huzmeli C, et al. (2008) Prognostic value of preoperative CEA, CA 19-9, CA 72-4, and AFP levels in gastric cancer. *Adv Ther* 25(10): 1075-1084.
17. Primrose JN (2008) Stomach and Duodenum. In: Williams NS, et al. (Eds.), *Bailey and Loves short practice of Surgery*, Arnold. (25th edn), International Student Edition, USA, pp. 1045-1079.
18. Islam SMJ, Ali SM, Ahmed S, Afroz QD, Chowdhury R, et al. (2009) Histopathologic Pattern of Gastric Carcinoma In Bangladesh *JAFMC Bangladesh* 1(5): 21-24.
19. Bold RJ, Ota MD, Ayani AJ, Mansfield PF (1999) Peritoneal & serum tumor markers predict recurrence and survival of patients with resectable gastric cancer. *Gastric Cancer* 2(1): 1-7.
20. Sougioultzis S, Syrios J, Xynos ID, Bovaretos N, Kosmas C, et al. (2011) Palliative gastrectomy and other factors affecting overall survival in stage IV gastric adenocarcinoma patients receiving chemotherapy: A retrospective analysis. *Eur J Surg Oncol* 37(4): 312-318.
21. Chowdhury SA, Hussain MM, Ahmed J (2010) Presentation and Immediate Outcome of Surgical Treatment of Patients with Carcinoma of the Stomach - A Comparative Study between Young and Elderly patients. *J Bangladesh Coll Phys Surg* 28(3): 145-150.
22. Hayes N, Wayman J, Wadehra V, Scott DJ, Raimes SA, et al. (1999) Peritoneal cytology in the surgical evaluation of gastric carcinoma. *Br J Cancer* 79(3-4): 520-524.
23. Fanelli MF, de Paiva TF, Silva MJ, Benevides CF, Guimarães AP, et al. (2009) Predictors of Peritoneal Carcinomatosis in Patients With Gastric Cancer Treated at a Single Institution in Brazil. *J Surg Oncol* 100(6): 452-455.
24. Rosenberg R, Nekarda H, Bauer P, Schenck U, Hoefler H, et al. (2006) Free peritoneal tumour cells are an independent prognostic factor in curatively resected stage IB gastric carcinoma. *Br J Surg* 93(3): 325-331.
25. Emoto S, Ishigami H, Yamashita H, Yamaguchi H, Kaisaki S, et al. (2012) Clinical significance of CA125 and CA72-4 in gastric cancer with peritoneal dissemination. *Gastric Cancer* 15(2): 154-161.
26. Adachi S, Noda T, Kiyozuka Y, Ito K, Itani Y, et al. (1994) The importance of CA125 immunohistochemical staining in patients with ovarian cancer. *Acta Obstet Gynaecol Jpn* 46: 896-902.
27. Dennis JL, Hvidsten TR, Wit EC, Komorowski J, Bell AK, et al. (2005) Markers of adenocarcinoma characteristic of the site of origin: development of a diagnostic algorithm. *Clin Cancer Res* 11(10): 3766-3772.