

ORIGINAL RESEARCH**Malignant Gastric Neoplasm and Its Peritoneal Metastases in Relation with CA 125 Levels: A Cross Sectional Study from a Tertiary Care Hospital of Bihar**

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Abstract:

Gastric cancer is a malignant tumor with a fifth position amid all cancers and its mortality rate is third, globally. But the frequency varies in several parts of the world. In India, amongst men it is the fifth most common cancer and in women it is in seventh position. The objective was to study the clinical significance of serum CA125 and its relation to PD in cases of gastric cancer. **Materials and Methods:** An observational study with cross-sectional design was conducted by the Department of Pathology, Indira Gandhi Institute of Medical Science, Patna, Bihar, India from May 2021 to April 2022 were studied. The study included samples from 25 patients during this duration. Approval from the Institutional Ethics Committee and written informed consent from the patients was taken. All the gastrectomy specimens were sent for gross examination, staging and histopathology. The paraffin embedded tissue blocks were subsequently stained for H&E. Microsoft excel 2016 and Statistical Package for the Social Sciences (SPSS) version 18 (SPSS, Inc. Chicago, IL, USA) was used for data analysis. **Results:** TNM staging was done. T3 stage (16, 53.3%) comprised the major bulk of the cases followed by T2 (7, 23.3%), T4 (5, 16.7%) and T1 (2, 6.7%). Likewise, N2 nodal staging (18, 60%) was leading followed by N0 (9, 30%), N1 (2, 6.7%) and N3 (1, 3.3%). Distal metastasis was noted among 36.7% (11 cases) of the cases with liver as the most common site of metastasis followed by PD, left supraclavicular lymph node, and multiple metastases. Majority of the cases were stage IIIA (17, 56.7%) and stage IV (12, 40%). **Conclusion:** Early detection of peritoneal disease will help the clinicians to stratify the treatment of gastric cancers and to decide whether to go for surgical or palliative intervention.

Key Words: Malignant Gastric Neoplasm, Peritoneal Metastases, CA 125 Levels

INTRODUCTION

Gastric cancer is a malignant tumor with a fifth position amid all cancers and its mortality rate is third, globally [1]. But the frequency varies in several parts of the world. In India, amongst men

it is the fifth most common cancer and in women it is in seventh position [2]. Multifactorial causation has an important role in gastric cancer which includes various dietary and environmental factors.

The most common distant mode of metastasis is PD. In such cases, a gastrectomy does not improve the prognosis but can rather hamper the patient's quality of life [3]. Also, PD is the most common recurrence pattern after curative gastrectomy with extended lymphadectomy [4]. Computed Tomography (CT) scan, Positron Emission Tomography (PET) and laparoscopic evaluation are commonly used to detect PD but they are either inconvenient or overly complex, so surgeons face to unforeseen non-curative operation [5]. Serum tumor markers are usually used for prompt diagnosis of tumor burden and occult metastases in variety of cancer patients. CA125 is an antigenic determinant detected by a murine monoclonal antibody OC125 [6]. Initially, it has been used primarily as a tumor maker for ovarian cancer. However, many new studies suggest that the peritoneum is an important source of CA125 and that there is a positive correlation between serum CA125 level and PD in cases of malignant gastric neoplasm [7-9]. Advanced gastric cancer with PD has poor prognosis and so early detection is necessary. The objective was to study the clinical significance of serum CA125 and its relation to PD in cases of gastric cancer.

Materials and Methods

An observational study with cross-sectional design was conducted by the Department of Pathology, Indira Gandhi Institute of Medical Science, Patna, Bihar, India from May 2021 to April 2022 were studied. The study included samples from 25 patients during this duration. Approval from the Institutional Ethics Committee and written informed consent from the patients was taken.

Inclusion criteria: All confirmed cases of malignant gastric neoplasm by endoscopic biopsy planned for gastrectomy and preoperative serum CA125 level done in confirmed malignant gastric neoplasm cases were included in the present study after taking proper informed consent.

Exclusion criteria: Cases with no preoperative serum CA125, received prior chemo-irradiation, critically ill patients unfit for surgery and those refused to give consent for the study were excluded.

Proper history, clinical examination, routine investigation was done according to the Performa. Rapid Urease Test (RUT) was also performed. Peripheral blood sample for CA125 assay was collected one week prior to surgery. The sera were analyzed using an immunoradiometric assay (ovarian cancer antigen (OD289), Omega Diagnostics Ltd., UK). The cut-off value of CA125 was 35U/mL according to the manufacturer's manual. This data was to be compared among the same patients diagnosed with PD. PD was identified through USG/CT or intraoperatively during open surgery. All the gastrectomy specimens were sent for gross examination, staging and histopathology. The paraffin embedded tissue blocks were subsequently stained for H&E.

Statistical Analysis

Microsoft excel 2016 and Statistical Package for the Social Sciences (SPSS) version 18 (SPSS, Inc. Chicago, IL, USA) was used for data analysis. Statistical forms were used to record the demographic, clinical, laboratory data of each patient. Chi-square test was used for the

comparison between the groups. Categorical values were expressed as rate with 95% Confidence Intervals (CI). A p-value of <0.05 was considered significant.

Results

This study comprised 30 cases. The mean age of the patients was 57.9 years with a SD of 18.3 years. Majority of the patients were in more than 50 years of age. Male comprised 19/30 cases included in the study population. The male to female ratio was 1.73:1.

Majority of the patients complained of anorexia followed by dyspepsia, pallor and hematemesis. Positive family history was present only in 2 cases. Other details of the study population has been given in Table 1.

Category	Sub-category	Number (%)
Clinical complaints	Anorexia	21 (70%)
	Dyspepsia	17 (56.7%)
	Pallor	16 (53.3%)
	Hematemesis	13 (43.3%)
Dietary history	Smoking	16 (53.3%)
	Alcohol	12 (40%)
	Fresh fruits/vegetables	9 (30%)
	Fermented fish/meat	7 (23.3%)
Gastrectomy specimen	Partial	18 (60%)
	Total	8 (26.7%)
	Subtotal	3 (10%)
	Total with splenectomy	1 (3.3%)
Site of stomach involved	Antral-pyloric	6 (20%)
	Antrum	12 (40%)
	Pylorus	4 (13.3%)
	Body	6 (20%)
	Cardia	1 (3.3%)
	Fundus	1 (3.3%)
Gross features by Borrmann classification [10]	Polypoid	14 (46.7%)
	Ulcerative	9 (30%)
	Infiltrative ulcerative	4 (13.3%)
	Diffuse infiltrative	3 (10%)
WHO classification of Adenocarcinoma [11]	Tubular (poorly differentiated)	14 (46.7%)
	Tubular (moderately differentiated)	9 (30%)
	Tubular (well differentiated)	3 (10%)
	Mucinous	2 (6.7%)
	Papillary	1 (3.3%)
	Signet ring cell type	1 (3.3%)

Table 1: Clinico-pathological characteristics of the cases.

TNM staging was done. T3 stage (16, 53.3%) comprised the major bulk of the cases followed by T2 (7, 23.3%), T4 (5, 16.7%) and T1 (2, 6.7%). Likewise, N2 nodal staging (18, 60%) was leading followed by N0 (9, 30%), N1 (2, 6.7%) and N3 (1, 3.3%). Distal metastasis was noted among 36.7% (11 cases) of the cases with liver as the most common site of metastasis followed by PD, left supraclavicular lymph node, and multiple metastasis. Majority of the cases were stage IIIA (17, 56.7%) and stage IV (12, 40%).

For PD among 13 (43.3%) cases, CA125 cut-off value ≥ 35 U/mL was used as a reference value [7]. Among 13 cases with PD, CA 125 value above cut-off was noted among 11 (84.6%) cases. For those without PD, CA 125 value above cut-off was seen among 5 out of 17 cases (29.4%). There was a significant correlation (p-value < 0.0001) with PD and CA125 serum assay.

Discussion

Gastric cancer is one of the most commonly observed malignant tumors. Incidence and the patterns of gastric cancer show a worldwide variation. High incidence is seen in countries of Southeast Asia, Japan and China as compared to India [11]. The age and gender distribution of the study population in our study was quite similar to the other studies [2, 12-14]. Majority of the patients complained of anorexia followed by dyspepsia, pallor and hematemesis. These clinical findings were comparable to the other studies [2,12-14]. Family history was present only in 2 cases. This estimate was low due to inadequate history given by the patients. Consumption of fermented fish/red meat and smoking was found among a considerable size of the study population. This was coherent with other studies [2,14]. As per RUT results, history of preceding H. pylori infection was seen in 6 cases (20%). Nandi A et al., RUT results showed 24.1% positivity [12]. The maximum palliative surgery was partial gastrectomy. Similar findings were seen with other studies [12,14,15]. Among the adenocarcinoma, the most common type was tubular (solid)-poorly differentiated. This was consistent with other studies [2,12-14].

Gastric carcinomas are a biologically and genetically heterogeneous group of tumors with multifactorial aetiologies. It occurs mostly in persons aged 30 years or more and incidence increases progressively with age in both men and women [16]. The common aetiology is smoking, dietary factors such as high intake of smoked meat, salt preserved food and low intake of fresh fruit and vegetables, H. pylori infection [17]. Histological types of adenocarcinoma are subclassified into different categories as tubular composed of slit-like and branching tubules, papillary has elongated finger-like supported by fibrovascular connective tissue cores, mucinous composed of extracellular mucin pools (>50%), signet ring cell type characterized by cytoplasmic mucin with an eccentrically placed nucleus and mixed is composed of glandular and signet ring/poorly cohesive cellular components. CK7, CK20, MUC6, CDX2 are specific for primary gastric adenocarcinomas [18]. The prognosis for advanced gastric cancer especially with PD is poor and the quality of life is also compromised. So, early diagnosis of the degree and extent of PD is essential. Nowadays, USG/CT is used to assess the PD. The specificity is high but the sensitivity is low and with a drawback in finding the nodules less than 5 mm [19]. Laparoscopic examination is well-precise but it is an invasive procedure. Nonetheless, current serum tumour markers can be easily and cost-effectively identified and can be useful for the preoperative staging of neoplasms, postoperative monitoring of treatment and early diagnosis of recurrence.

Tumour marker is selectively secreted by cancer cells alone, in the blood or in other body fluids. CA125 is a repeating peptide epitope of the mucin MUC16 and is identified as a 5797-base pair cDNA isolated from the OVCAR-3 cDNA library [20]. Promoting cancer cell proliferation and

inhibiting anticancer immune responses are its biological function. CA125 is formerly found as a distinctive biological marker for ovarian cancer and is considered to be a method for detection of gastric cancer [21]. CA125 is also related to ovarian, uterine, lung and pancreatic cancers [22]. Some studies have shown that Systemic Inflammatory Response (SIR) and fibrinogen also plays an important role in tumor progression and metastasis in advanced gastric cancer [23-25].

Conclusion

Gastric cancer is one of the most common cancers worldwide and remains to be an important malignant disease with significant geographical, ethnic and socio-economic difference in distribution. Majority of malignant gastric neoplasms are asymptomatic and hence, presents in late stage. Early detection of peritoneal disease will help the clinicians to stratify the treatment of gastric cancers and to decide whether to go for surgical or palliative intervention.

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