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POSITIVE PERITONEAL WASH CYTOLOGY IN INTRA-ABDOMINAL MALIGNANCIES – A CROSS - SECTIONAL STUDY

Gastroenterology

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ABSTRACT

Peritoneum is a frequent site for recurrence post-resection in intra-abdominal malignancies. Positive Peritoneal wash cytology (CY+) may have significant prognostic implications, influencing staging, treatment decisions, and management. **Objective:** To determine the prevalence of CY+ in patients undergoing curative resection for intra-abdominal malignancies and evaluate its correlation with biomarkers, including, CEA, CA 19-9, and the platelet-lymphocyte ratio (PLR). **Methodology:** A cross-sectional observational study was conducted over 18 months (2022-2024) at the Department of Surgical Gastroenterology, Medical College, Trivandrum, Kerala, India, a tertiary care center. The study included 215 consecutive patients with clinically and/or radiologically proven intra-abdominal malignancies who were eligible for potential curative resection. Gynecological or retroperitoneal malignancies, negative final histopathological results, or intraoperative gross peritoneal deposits were excluded. Data on demographics, clinical examination, blood investigations, imaging, biopsy, and histopathological and cytopathological reports were analyzed using SPSS software. **Main outcome:** CY+ was observed in 5.11% (11/215) of patients, with 2.79% (6/195) in the curative resection group and 25.0% (5/20) in the palliative resection group. **Results:** Among the 215 patients, 128 (59.53%) were males and 87 (40.46%) females, with mean age of 59.9 (28–87, σ =10.59). This included colorectal 116(53.95%), periampullary/pancreatic 53(24.65%), gastric 16(7.44%), gastroesophageal junction 14(6.51%), hepatobiliary 13(6.04%), and small bowel malignancies 3(1.39%). CY+ was observed in 5.11% of patients, all of whom in the curative group (2.79%) also had lymph node metastases and received adjuvant therapy. CEA >7.56 (81.82% sensitivity, 84.31% specificity), CA 19-9 >38 (81.82% sensitivity, 80.39% specificity), and PLR >150 were significantly associated with CY+ ($p = 0.01$). **Conclusion:** CY+ was detected in 2.79% of curative resection, all of whom also had lymph node metastases. CY+ did not independently influence the decision for adjuvant treatment. PLR >150, CEA >7.56, or CA-19.9 >38 indicate higher risk for occult peritoneal metastasis independent of lymph node status.

KEYWORDS

Peritoneal wash cytology, intra-abdominal malignancies, CEA, CA 19-9, PLR

1. INTRODUCTION

Despite advancements in early cancer detection, many patients are diagnosed at advanced stages, and many experience recurrence even after seemingly curative resections(R0). Peritoneal metastases, whether present at diagnosis or recurrence, are a frequent observation in intra-abdominal malignancies. Positive peritoneal wash cytology detects malignant cells in the peritoneal cavity, offering crucial staging information, reflecting tumor cell dissemination into the peritoneum via direct shedding from the serosal surface or through lymphatic vessels in the submucosal layer.

First used for gynecologic cancers in 1956(1), the concept has now been extended to various malignancies. In gastric cancer, it indicates M1 disease (AJCC Stage IV), with a 5-year survival rate of 2% and a median survival of 9.2 months(2–4). Positive peritoneal cytology also predicts survival in colorectal(5–8)and pancreatic cancers(9–11). Only a limited number of studies have extensively detailed the use of peritoneal wash cytology in hepatobiliary malignancies. A study conducted by Matsukuma et al. concluded the positive status of peritoneal lavage cytology could moderately affect the survival of patients with biliary tract cancers(12). Additionally, peritoneal wash cytology has been utilized in cholangiocarcinoma for molecular profiling, identifying therapeutic targets like pemigatinib and ivosidenib and resistance mechanisms(13). Thus, detection of malignant cells in peritoneal washings can influence treatment, leading to intraperitoneal chemotherapy, aggressive systemic therapy, or clinical trial enrollment. Despite its clinical utility, regional data on CY+ remains limited, prompting this study.

2. MATERIALS AND METHODS

A single-center, cross-sectional observational study analyzed the prevalence and prognostic value of CY+ in patients undergoing curative resection for intra-abdominal malignancies. Approved by the Institutional Ethics Committee, the study was conducted at the Department of Surgical Gastroenterology, Medical College, Trivandrum, from 2022 to 2024.

2.1 Patients and Study Design

Clinical, radiological, and pathological data from 215 consecutive patients with clinically and/or radiologically proven intra-abdominal malignancies being considered for potential curative resection were analyzed. Exclusions included patients with gynecological or retroperitoneal malignancies, negative final histopathological results, or intraoperative peritoneal deposits. Data collected included age, sex, preoperative therapy (Neoadjuvant chemotherapy and/or radiotherapy), preoperative serum carcinoembryonic antigen (CEA) levels, serum carbohydrate antigen 19-9 (CA19-9) levels, platelet-lymphocyte ratio (PLR), and operative procedure. Radiological data included tumor staging. Pathological data included peritoneal wash cytology status and TNM staging, according to the 8th edition of the Classification of Malignant Tumours by the Union for International Cancer Control(14).

2.2 Peritoneal Wash Cytology

Peritoneal wash cytology was performed during laparoscopy or open resection. Prior to tumor manipulation, 500ml of warm saline was instilled into the peritoneal cavity—100ml each into the Douglas pouch, bilateral paracolic gutters, and the right and left subphrenic spaces—and manually stirred. After a brief 10-minute holding period, 50 ml of fluid was recovered. In patients with on-table ascites, 50 ml of ascitic fluid was collected instead, and no wash was performed. The samples were sent for cytopathological analysis, where they were centrifuged for 5 minutes at 2000 rpm. The resulting cell button was further centrifuged with 2–3 drops of supernatant fluid for 10 minutes at 2000 rpm. The sediment was smeared and stained using Papanicolaou's method and Giemsa stain. All cytological examinations were carried out by a designated cytopathologist. Cytological findings were classified as either positive or negative.

2.3 Statistical Analysis

Continuous variables were analyzed using the Mann-Whitney U test, while categorical variables used the chi-square test. Diagnostic performance was assessed via ROC curves, with p-values <0.05 considered significant. Analyses were performed using IBM SPSS Statistics, version 26 (IBM Corp., Armonk, NY, USA)

3. RESULTS

215 patients (128 males, 87 females;mean age 59.9 years, standard deviation = 10.59) were qualified for the study. The malignancies in these patients were categorized as follows: colorectal cancer 116 (53.95%), periampullary/pancreatic cancer 53 (24.65%), Gastric cancer 16 (7.44%), gastroesophageal (GE) junction cancer 14 (6.51%), hepatobiliary malignancies 13 (6.04%), and small bowel malignancies 3 (1.39%). 195 (90.69%) underwent curative resections, while 20 (9.30%) who were initially planned for curative resection underwent palliative procedures due to the advanced nature of their disease discovered intraoperatively. (Table 1)

Table 1- Clinical Demographic Characteristic Of Patients

Characteristic	Number of participants	Percentage
Gender		
Male	128	59.53
Female	87	40.46
Malignancies		
Colorectal	116	53.95
Periampullary/Pancreatic cancer	53	24.65
Gastric cancer	16	7.44
Gastroesophageal junction cancer	14	6.51
Hepatobiliary malignancies	13	6.04
Small bowel malignancies	3	1.39
Surgical Procedure		
Curative resection	195	90.69
Palliative procedure	20	9.30
Peritoneal wash Cytology status		
Positive	11	5.11
Negative	204	94.88
Lymph node involvement in curative group		
Present	128	65.64
Absent	67	34.35

3.1 Positive Peritoneal Wash Cytology (CY+)

CY+ was observed in 11 patients (5.11%) of the total cohort. (Fig 1) Within the subgroup of patients who underwent curative resection, 6 out of 195 patients (2.79%) had CY+. Conversely, in the subgroup of patients who underwent palliative procedures, 5 out of 20 patients (25.0%) had CY+. The Chi-square analysis demonstrated a significant correlation between CY+ and palliative procedures ($\chi^2 = 17.959$, $p < 0.0001$).

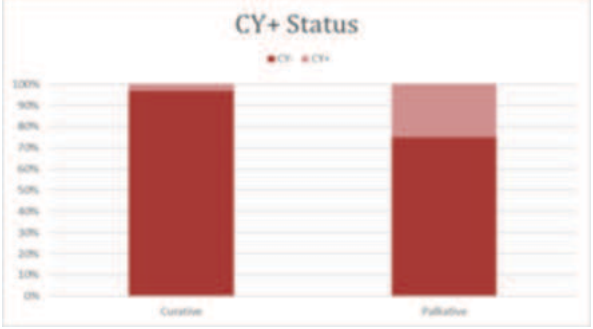

Fig 1- Bar Diagram Showing CY+ status

In the curative resection group, among 195 patients, CY+ was found in 5 colorectal and 1 gastric cancer patient. Among the 20 palliative cases, CY+ was identified in 2 pancreatic, 1 gastric, 1 hepatobiliary, and 1 gastroesophageal junction cancer patient.

Among 195 patients undergoing curative resection, 128 had lymph node metastasis including all 6 CY+ cases, indicating CY+ did not independently affect the decision to pursue adjuvant therapy. The lymph node metastases— an established indication for adjuvant therapy—was the primary determinant.

3.2 Relation Between CY+ and Tumor Markers

The study identified strong associations between positive peritoneal wash cytology (CY+) and elevated tumor markers, Carcinoembryonic antigen (CEA) and Carbohydrate Antigen 19-9 (CA 19-9). ROC analysis showed good predictive value, with CEA (AUC = 0.799, p = 0.0007) and a threshold >7.56 yielded 81.82% sensitivity and 84.31% specificity for predicting CY+ (Fig 2). Similarly, CA 19-9 (AUC = 0.815, $p < 0.0001$) and a threshold >38 showed 81.82% sensitivity and 80.39% specificity (Fig 2). These markers can aid in early detection of occult metastases, guiding risk stratification. Further research in this area may help identify patients at high-risk, and possibly define indications for neoadjuvant therapy.

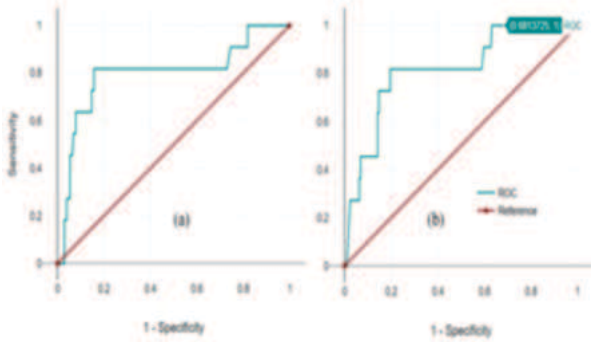

Fig 2. Receiver Operating Curve Plotted Between CEA (a), CA19.9 (b) and CY+ status

3.3 Relation Between CY+ and Platelet-Lymphocyte Ratio (PLR)

Platelet-Lymphocyte Ratio (PLR) has become an important marker in various cancers, including intra-abdominal malignancies(15). This study found that a PLR exceeding 150 was significantly associated with CY+ (p = 0.01). This result is consistent with previous research linking high PLR to worse outcomes in colorectal, gastric, and liver cancers(16–19). Elevated PLR reflects inflammation that can enhance tumor growth and metastasis. This finding highlights the role of inflammation in cancer progression suggesting that integrating PLR into diagnostics could identify patients at high risk for peritoneal involvement, guiding more tailored treatment strategies like neoadjuvant therapy.

1. DISCUSSION

Positive peritoneal wash cytology (CY+) is a pivotal indicator of disease spread in intra-abdominal malignancies, underscoring its strong prognostic significance, particularly in advanced tumour stages. For instance, in gastric cancer, CY+ is classified as M1 disease (Stage IV), with a median survival time of 9.2 months and a 5-year survival rate of only 2%(2–4). Hoshimoto et al. demonstrated that the presence of positive cytology was correlated with reduced survival rates in pancreatic malignancies(9). Similarly, Aoki et al. examined the prognostic impact of intraoperative peritoneal cytology following neoadjuvant therapy in pancreatic malignancies(10)

The use of peritoneal wash cytology in hepatobiliary malignancies has been less extensively studied. Research on intrahepatic and extrahepatic cholangiocarcinoma has also employed peritoneal wash cytology to obtain cells for molecular profiling, aiding in the identification of therapeutic targets and resistance mechanisms to treatments like pemigatinib and ivosidenib.

In colorectal cancer, positive peritoneal cytology has been shown to predict poorer survival outcomes.

In this study, all CY+ patients in the curative resection group also had lymph node metastasis (LN+), indicating that CY+ status did not influence the decision for adjuvant therapy, as the presence of LN+

either way warranted additional treatment. Our treatment protocol did not involve HIPEC for CY+ cases, and due to logistical constraints, obtaining intraoperative cytology results in real-time was not feasible, which could have otherwise aided in making intra-operative surgical modifications.

Carcinoembryonic antigen (CEA) and Carbohydrate Antigen 19-9 (CA 19-9), commonly used biomarkers for detecting and monitoring intra-abdominal malignancies, showed strong predictive value for CY+ status. The ROC curve analysis demonstrated that CEA level greater than 7.56 provided 81.82% sensitivity and 84.31% specificity and CA 19-9 value greater than 38 yielding 81.82% sensitivity and 80.39% specificity for predicting CY+.

Additionally, this study found that a platelet-lymphocyte ratio (PLR) greater than 150 was significantly associated with CY+ status ($p = 0.01$), consistent with previous studies linking elevated PLR to poorer prognosis in colorectal, gastric, and liver cancers (16–19) and supporting the role of inflammation in cancer progression and metastasis.

The study's findings have key clinical implications. The strong link between CY+ status and advanced disease underscores the importance of early detection and aggressive treatments like neoadjuvant therapy or HIPEC. Although CY+ did not affect adjuvant therapy decisions in our study, it remains a vital marker of disease progression. Additionally, correlations with CEA, CA 19-9, and PLR suggest these biomarkers aid in detecting high-risk patients and tailoring treatment strategies. Despite its findings, the study has limitations. Single-center design, inability to perform intraperitoneal chemotherapy, logistical issues affecting intraoperative cytology, and lack of long-term survival data can affect generalizability of the findings.

CONCLUSION

Positive peritoneal wash Cytology (CY+) was detected in 2.79% of patients undergoing curative resection, all of whom also exhibited lymph node metastases. CY+ did not independently influence the decision for adjuvant treatment in this study. In contrast, 25% of patients undergoing palliative procedures were CY+. High-risk markers for occult peritoneal metastasis include PLR >150, CEA >7.56, or CA-19.9 >38, spotlighting the need to proactively look out for peritoneal disease in these patients.

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Conflict of Interest

The authors declare no conflicts of interest.

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