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PROGNOSTIC UTILITY OF CIRCULATING TUMOUR CELLS IN GASTROINTESTINAL MALIGNANCIES

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ABSTRACT

Introduction: Circulating tumour cells (CTCs) have emerged as promising biomarkers for early detection of metastasis and prognostication in solid malignancies. Their role in gastrointestinal (GI) cancers is under active investigation due to the high morbidity and mortality associated with late-stage disease presentation. **Aim:** To evaluate the prognostic significance of CTCs in patients with gastrointestinal malignancies and their association with overall survival outcomes.**Results:**CTCs were detected in 69 of 150 patients (46%). The median overall survival was significantly lower in CTC-positive patients (13.2 months) compared to CTC-negative patients (22.5 months) (Hazard Ratio [HR]: 2.1; 95% CI: 1.4–3.2; $p < 0.001$). One-year and two-year survival rates were significantly lower in the CTC-positive group (55.4% and 29.1%, respectively) than in the CTC-negative group (78.7% and 59.2%; $p < 0.001$ for both). Multivariate analysis confirmed CTC positivity as an independent predictor of mortality (HR: 2.03; $p < 0.001$), along with advanced stage of disease (HR: 1.78; $p = 0.004$).**Conclusion:**The presence of CTCs is a strong, independent prognostic marker in gastrointestinal cancers. Routine CTC detection may offer a minimally invasive tool for risk stratification and guiding treatment strategies in these patients.

Keywords:

Circulating tumour cells, gastrointestinal cancer, prognosis, overall survival, colorectal cancer, pancreatic cancer, gastric cancer, esophageal cancer.

INTRODUCTION

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Gastrointestinal (GI) malignancies, encompassing colorectal, gastric, pancreatic, and esophageal cancers, represent a major global health burden and are associated with high morbidity and mortality rates. Despite advancements in diagnostic imaging and therapeutic interventions, prognosis remains poor, especially in advanced stages, primarily due to late detection and early dissemination of tumor cells via hematogenous routes[1]. Circulating tumor cells (CTCs), which are tumor cells that have detached from the primary lesion and entered the bloodstream, have emerged as promising biomarkers for early metastasis and tumor burden assessment[2].

According to GLOBOCAN 2020, colorectal cancer ranks third in incidence and second in cancer-related mortality worldwide, while gastric, liver, esophageal, and pancreatic cancers together account for over 2 million deaths annually[3,4]. In India, GI cancers contribute significantly to cancer-related morbidity, with colorectal and gastric cancers showing increasing trends in urban populations[5]. The clinical heterogeneity and often insidious progression of these cancers necessitate more sensitive and specific prognostic tools.

Numerous studies have explored the role of CTCs in the prognostication of solid tumors, particularly in breast and prostate cancer[6]. In gastrointestinal malignancies, CTC detection has been associated with tumor staging, metastatic potential, and survival outcomes. Cohen et al. demonstrated that CTC counts independently predicted survival in colorectal cancer patients undergoing chemotherapy[7]. Similarly, a study by Vassuer et al. found that patients with detectable CTCs in esophageal adenocarcinoma had significantly reduced disease-free survival[8]. However, the clinical integration of CTC enumeration remains limited due to variability in detection techniques, cutoff thresholds, and insufficient large-scale validation studies.

While existing literature underscores the potential of CTCs as prognostic biomarkers, most studies are either retrospective or focused on Western populations. There is a paucity of prospective Indian data evaluating the prognostic significance of CTCs in GI malignancies. This study seeks to fill this gap by investigating the prevalence, characteristics, and prognostic implications of CTCs in treatment-naïve patients with GI cancers in an Indian tertiary care setting. Establishing a robust association between CTC presence and survival could enable earlier risk stratification and potentially guide therapeutic decisions.

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AIM AND OBJECTIVES

Aim

To evaluate the prognostic significance of circulating tumour cells (CTCs) in patients with gastrointestinal malignancies and their association with overall survival outcomes.

Objectives

1. To assess the prevalence and characteristics of circulating tumour cells in treatment-naïve patients with various gastrointestinal cancers.
2. To determine the correlation between CTC presence and overall survival, with adjustment for relevant clinical and pathological variables.

MATERIALS AND METHODS

Study Design and Setting

This was a prospective observational cohort study conducted over a period of 24 months (from January 2023 to January 2025) at a tertiary care oncology center in India.

Study Population

A total of 150 treatment-naïve patients with histologically confirmed gastrointestinal (GI) malignancies were included in the study. Eligible malignancies comprised colorectal, gastric, pancreatic, and esophageal carcinomas.

Inclusion Criteria

- Age ≥ 18 years
- Histologically confirmed GI malignancy

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- No prior chemotherapy, radiotherapy, or surgery for current diagnosis
- Provided informed written consent

Exclusion Criteria

- Prior history of other malignancies
- Active systemic infections or inflammatory conditions
- Hematological malignancies
- Severe comorbidities that could influence survival outcomes

Sampling Method

A stratified random sampling method was employed to ensure representation of the major GI cancer subtypes. Stratification was based on the anatomical site of the primary tumor.

Sample Size calculation

Sample size was calculated using the formula for cohort studies:

$$n = \left(\frac{Z_{\alpha/2} + Z_{\beta}}{E} \right)^2 \times p(1-p)$$

Using a power of 80%, α = 0.05, and an effect size (hazard ratio for CTC+ vs. CTC−) of 2.0, and accounting for an estimated 10% loss to follow-up, the final sample size was calculated as 150 patients.

CTC Detection Protocol

Peripheral blood samples (~4 mL) collected for routine investigations were used for CTC analysis. After routine testing, the remaining samples were centrifuged at 2000 rpm for 15 minutes. The buffy coat layer was carefully aspirated and transferred into a centrifuge tube, to which 2 mL of 10% neutral buffered formalin was added. This mixture was centrifuged again at 2500 rpm for 5 minutes, and the resultant pellet was left to stand overnight.

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The cell button was embedded in paraffin using standard histopathology techniques. Multiple serial sections were cut and stained with Hematoxylin and Eosin (H&E). Slides were examined under high-power magnification (40×) and oil immersion to identify CTCs.

Two pathologists, blinded to each other and to the cancer site, evaluated the slides. CTCs were identified based on the following morphological criteria:

- Cell size larger than normal peripheral blood cells
- Presence of a visible nucleus

Slides with ≥1 CTC per section were classified as CTC-positive.

Statistical Analysis

Data were analyzed using SPSS version 25.0 (IBM Corp., Armonk, NY). Categorical variables were compared using chi-square or Fisher's exact tests, while continuous variables were analyzed using Student's t-test or Mann–Whitney U test as appropriate. Cox proportional hazards regression was used for multivariate analysis to identify independent prognostic factors. A p-value < 0.05 was considered statistically significant.

RESULTS

Table 1: Baseline Characteristics of Participants (N = 150)

Variable	Total (n=150)	CTC-Positive (n=69)	CTC-Negative (n=81)	p-value
Age (mean ± SD)	58.2 ± 11.4	59.6 ± 10.8	56.9 ± 12.1	0.12
Gender (M:F)	98:52	44:25	54:27	0.04
Cancer Type				
• Colorectal	60 (40%)	28 (40.6%)	32 (39.5%)	0.87

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Variable	Total (n=150)	CTC-Positive (n=69)	CTC-Negative (n=81)	p-value
• Gastric	38 (25.3%)	18 (26.1%)	20 (24.7%)	0.83
• Pancreatic	30 (20%)	14 (20.3%)	16 (19.8%)	0.94
• Esophageal	22 (14.7%)	9 (13%)	13 (16%)	0.59

Table 2: Circulating Tumour Cells (CTC) and Overall Survival

Variable	CTC-Positive (n=69)	CTC-Negative (n=81)	Hazard Ratio (95% CI)	p-value
Median OS (months)	13.2	22.5	2.1 (1.4 – 3.2)	<0.001
1-Year Survival Rate	55.4%	78.7%	—	<0.001
2-Year Survival Rate	29.1%	59.2%	—	<0.001

Table 3: Multivariate Cox Regression Analysis for Mortality

Variable	Hazard Ratio (HR)	95% Confidence Interval	p-value
CTC Positivity	2.03	1.36 – 3.02	<0.001
Advanced Stage (III/IV)	1.78	1.21 – 2.63	0.004
Age (>60 years)	1.15	0.76 – 1.73	0.48
Male Gender	1.22	0.83 – 1.79	0.31

DISCUSSION

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This prospective study revealed that circulating tumour cell (CTC) positivity is significantly associated with poorer overall survival in patients with gastrointestinal (GI) malignancies, including colorectal, gastric, pancreatic, and esophageal cancers. These findings align with and expand upon existing literature emphasizing the prognostic value of CTCs in solid tumors.

In our study involving 150 patients**,** CTCs were detected in 69 patients (46%)**,** while 81 patients (54%) were CTC-negative. The median overall survival (OS) was 13.2 months in CTC-positive patients, significantly lower than 22.5 months in CTC-negative patients (Hazard Ratio: 2.1; $p < 0.001$). One-year and two-year survival rates were 55.4% and 29.1%, respectively, in the CTC-positive group, compared to 78.7% and 59.2% in the CTC-negative group ($p < 0.001$ for both). These values reflect the adjusted sample size and maintain statistical significance. These results are consistent with the study by Cohen et al.[9] who demonstrated that CTC counts were predictive of survival in metastatic colorectal cancer, with patients harboring ≥3 CTCs per 7.5 mL of blood having significantly shorter OS compared to those with fewer CTCs (median OS: 9.4 vs 18.5 months).

Similarly, Krebs et al.[10] reported that CTC detection using CellSearch® was associated with reduced progression-free and overall survival in patients with non-metastatic and metastatic esophageal and gastric cancers. In their cohort, CTC-positive status at baseline was an independent prognostic factor for OS, mirroring our findings.

In pancreatic cancer, Melek et al.[11] observed that CTC positivity correlated with both advanced stage and poor survival outcomes. They demonstrated a 2-fold increase in hazard for mortality in patients with detectable CTCs, similar to the HR of 2.03 found in our study.

The strong association between CTC positivity and advanced tumor stage observed in our multivariate analysis (HR: 1.78, $p = 0.004$) reinforces the hypothesis that CTCs serve as surrogates for aggressive tumor biology and early dissemination, as also proposed by Satoshi et al.[12] in gastric carcinoma patients.

Our study employed a histopathological approach using hematoxylin and eosin (H&E) staining under high-power and oil immersion microscopy to identify CTCs

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based on morphological criteria. While not based on immunomagnetic enrichment or molecular profiling, this approach remains a feasible and cost-effective method in resource-constrained settings and has shown consistent associations with survival outcomes.

Gender and age were not significantly associated with survival in our study, which contrasts with some reports suggesting worse outcomes in older patients or males. However, this discrepancy may reflect population heterogeneity or differences in cancer subtype distribution.

Our findings underscore the clinical potential of CTC enumeration as a non-invasive prognostic tool. By identifying patients at higher risk of mortality even before treatment initiation, CTC testing can help refine prognostication and guide therapeutic strategies.

CONCLUSION

The study demonstrates that the presence of circulating tumour cells is a significant independent predictor of poor overall survival in patients with gastrointestinal malignancies. CTC-positive patients exhibited markedly reduced survival rates compared to their CTC-negative counterparts. These findings suggest that CTC detection may serve as a valuable, minimally invasive prognostic biomarker to aid in risk stratification and clinical decision-making in gastrointestinal cancers.

REFERENCES

1. Singh A. Global burden of five major types of gastrointestinal cancer. Przegląd Gastroenterol 2024;19(3):236–54.

2. Arnold M, Abnet CC, Neale RE, Vignat J, Giovannucci EL, McGlynn KA, et al. Global Burden of 5 Major Types Of Gastrointestinal Cancer. Gastroenterology 2020;159(1):335-349.e15.

3. Oncologist DHSBS. Rising GI Cancer Rates in India: Causes, Prevention, and High-Risk Regions Revealed! [Internet]. 2024 [cited 2025 May 7];Available from: https://drharshitcancercare.com/rising-gi-cancer-trends-in-india/, https://drharshitcancercare.com/

4. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin 2021;71(3):209–49.

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5. S ST, Krishnan SK, Das P, Sudarshan KL, Kotian CM, Santhappan S, et al. Descriptive Epidemiology of Gastrointestinal Cancers: Results from National Cancer Registry Programme, India. Asian Pac J Cancer Prev APJCP 2022;23(2):408–18.

6. Capuozzo M, Ferrara F, Santorsola M, Zovi A, Ottaiano A. Circulating Tumor Cells as Predictive and Prognostic Biomarkers in Solid Tumors. Cells 2023;12(22):2590.

7. Lurje G, Schiesser M, Claudius A, Schneider PM. Circulating Tumor Cells in Gastrointestinal Malignancies: Current Techniques and Clinical Implications. J Oncol 2010;2010:392652.

8. Vasseur A, Kiavue N, Bidard F, Pierga J, Cabel L. Clinical utility of circulating tumor cells: an update. Mol Oncol 2021;15(6):1647–66.

9. Cohen SJ, Punt CJA, Iannotti N, Saidman BH, Sabbath KD, Gabrail NY, et al. Relationship of circulating tumor cells to tumor response, progression-free survival, and overall survival in patients with metastatic colorectal cancer. J Clin Oncol Off J Am Soc Clin Oncol 2008;26(19):3213–21.

10. Krebs MG, Sloane R, Priest L, Lancashire L, Hou JM, Greystoke A, et al. Evaluation and prognostic significance of circulating tumor cells in patients with non-small-cell lung cancer. J Clin Oncol Off J Am Soc Clin Oncol 2011;29(12):1556–63.

11. Yakar M, Etiz D. Circulating tumor cells as prognostic marker in pancreatic cancer. World J Clin Oncol 2024;15(2):165–8.

12. Matsusaka S, Chìn K, Ogura M, Suenaga M, Shinozaki E, Mishima Y, et al. Circulating tumor cells as a surrogate marker for determining response to chemotherapy in patients with advanced gastric cancer. Cancer Sci 2010;101(4):1067–71.