Original Article

Frequency of Thrombocytosis and Elevated C- Reactive Protein Levels in Different Stages of Esophageal Carcinoma in a Tertiary Care Hospital of Karachi

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ABSTRACT

Objective: To determine frequency of thrombocytosis and elevated C- reactive protein levels in different stages of esophageal carcinoma in a tertiary care hospital of Karachi.

Study Design: Descriptive, Cross –Sectional study

Place and Duration of Study: This study was conducted at the Surgical unit 05, Civil Hospital Karachi from 27 February 2018 to 26 February 2019.

Materials and Methods: A total of 97 patients with esophageal carcinoma on histopathology were included in the study. Diagnosed cancer patients were further assessed for stage of tumor via radiological investigations like Computed tomography scan Chest+ Abdomen with contrast and Endoscopic ultrasound. Platelet counts and C-Reactive protein levels was assessed in different stages of esophageal carcinoma using Tumor Nodal Metastasis staging system for esophageal cancer.

Results: The average age was 48.88±10.13 years. Frequency of elevated C- reactive protein and platelet count in esophageal carcinoma were observed in 73(75.26%) and 31(31.96%) while both were elevated in 29(29.9%) cases. Elevated CRP was significantly high in stage 3 and 4 esophageal carcinomas (p=0.0005) while and platelet count (> 400,000/Liter called thrombocytosis) were not statistically significant among stages of esophageal carcinoma (p=0.878).

Conclusion: Our findings confirmed that CRP may be used as an adjunct in evaluating the tumor markers in the diagnosis of EC patients. Since CRP is a sensitive, but nonspecific marker of inflammation, it might be helpful in the evaluation of EC.

Key Words: Esophageal carcinoma, Thrombocytosis, Elevated C- reactive protein

Citation of article: Taj A, Gul A, Jawed O, Ejaz S, Ahmed SSI, Shaikh N. Frequency of Thrombocytosis and Elevated C- Reactive Protein Levels in Different Stages of Esophageal Carcinoma in a Tertiary Care Hospital of Karachi. Med Forum 2023;34(9):92-95. doi:10.60110/medforum.340921.

INTRODUCTION

Esophageal carcinoma ranks as the eighth most prevalent malignancy worldwide[1]. It holds the unfortunate distinction of being the sixth leading cause of cancer-related mortality[2], with its incidence demonstrating significant geographical, racial, and socioeconomic disparities[3]. Notably, it is strikingly more common in certain regions, such as Northern China and Northern Iran, where the annual incidence approaches 100 per 100,000 population[4]. In contrast, the Western world reports a comparatively lower incidence, ranging between 10 to 20 per 100,000 per annum[5]. In Pakistan, esophageal carcinoma stands as the fifth most common tumor among females and the ninth among males[6], with a prevalence rate of 5 per 100,000 in Karachi[7]. Over the past three decades, the incidence of carcinoma has seen a steady increase[1]. Although esophageal carcinoma is typically a disease of the elderly, it occurs at a younger age in endemic regions[6]. Furthermore, it is notably more prevalent among males, with a male-to-female ratio of 3 to 4 times[8].

The prognosis of esophageal carcinoma is heavily contingent on the disease's stage at the time of diagnosis[9-11]. However, its role in esophageal carcinoma has yielded conflicting reports. While some studies, such as Shimada et al.[12], have associated thrombocytosis with advanced tumor stages and consequently poorer prognosis, others contend that

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Received: January, 2023
Accepted: March, 2023
Printed: September, 2023

platelet count does not serve as a reliable predictor of esophageal cancer prognosis[14].

Studies suggest that elevated CRP levels correlate with larger tumor size, tumor progression, lymph node metastasis, advanced stages, and poor prognosis among esophageal carcinoma patients[12]. In one study, the incidence of thrombocytosis and elevated CRP levels was found to be 50%, with 80% of thrombocytosis cases concurrently exhibiting elevated CRP levels. Traditional tumor staging involves clinical examination, imaging, and histopathological examination of resected specimens. Pre-treatment platelet counts and C-reactive protein measurements may complement radiological investigations in assessing tumor stage and planning management strategies. Esophageal cancer is a highly aggressive malignancy, with a dismal overall cure rate of less than 10% [17]. At presentation, systemic disease is detected in over 50% of cases, rendering them incurable. Surgical resection remains the accepted standard of care for localized disease, while neoadjuvant chemoradiotherapy, administered as a combined modality therapy, yields pathological responses in 20-40% of cases, serving as a potential surrogate marker for cure.

MATERIALS AND METHODS

Calculated sample size was 97 patients. Data was collected through non-probability-consecutive sampling.

Inclusion criteria: 30-70 years old patients (since cancer is more prevalent in this age (83)) both male and females diagnosed as case of esophageal carcinoma on histopathology was included in the study. Informed written consent was taken by the each participant prior to inclusion in this study by principle researcher.

Exclusion Ccriteria: Following factors was excluded from study since they all causes increase or decrease level of platelet count and C - reactive protein levels.

- Documented history of any infectious diseases like tuberculosis.
- Abnormal liver function tests (as defined in operational definition).
- Documented history of hepatitis B and hepatitis C.
- Documented history of Splenectomy.
- Documented history of collagen vascular disease & any inflammatory disorder like inflammatory bowel diseases.
- Documented history of myeloproliferative disorders.
- All co-morbid conditions like documented history of Diabetes Mellitus of any duration.

Data collection procedure: All patients coming to out-patient department with complain of dysphagia for solids/ liquids was assessed for esophageal carcinoma with Upper Gastrointestinal endoscopy & biopsy, endoscopy was done by professor of surgery of surgical unit 6, civil hospital Karachi and biopsy was sent to single pathologist of DOW laboratory. Diagnosed cancer patients were further assessed for stage of tumor via radiological investigations like Computed tomography scan Chest+ Abdomen with contrast and Endoscopic ultrasound (in early stages like stage I disease) by single consultant radiologist of civil hospital Karachi.

Platelet Counts: Early morning fasting blood samples was obtained from venipuncture site. Three milliliters of blood was collected in a clean EDTA glass container and platelets was counted in an automated optical counting machine (SYSMEX XN -1000) at civil hospital Karachi laboratory. The platelet count of > 400,000/Liter was taken as thrombocytosis.

C - reactive protein Levels: From each patient, 2 ml blood was collected in a clean glass container and quantitative C-reactive protein levels was performed by Cobas c- 501 at civil hospital Karachi laboratory. >5 mg/dl was taken as elevated levels. Platelet counts and C- Reactive protein levels was assessed in different stages of esophageal carcinoma using Tumor Nodal Metastasis staging system for esophageal cancer.

Data analysis procedure: Data was entered and analyzed using SPSS version 22. Frequency and percentages was find out for gender, stage of carcinoma, raised CRP and thrombocytosis. Age, CRP level, platelet count and duration of carcinoma were expressed as mean ± standard deviation.

RESULTS

A total of 97 patients with esophageal carcinoma on histopathology were included in the study. The average age was 48.88±10.13 years similarly average PLT, CRP level and duration of esophageal carcinoma is also reported in table 5.

Table No. 1: Descriptive Statistics Of Patients

Variables	Mean	SD	95% Confidence Interval for Mean	
			Lower Bound	Upper Bound
Age (Years)	48.88	10.13	46.83	50.92
PLT	346020.62	117187.08	322402.19	369639.04
CRP	24.275	32	17.826	30.725
Duration of Esophageal Carcinoma (Months)	5.04	2.44	4.55	5.53

Table No. 2: Compare the Frequency of Elevated Crp in Different Stages of Cancer

Elevated CRP	TNM Stage of Tumor			P-Value
	Stage 1 and 2	Stage 3 n=55	Stage 4 n=22	

	n=20			
Yes	8(40%)	49(89.1%)	16(72.7%)	0.0005
No	12(60%)	6(10.9%)	6(27.3%)	

Chi-Square= 19.08

Table No. 3: Compare the Frequency of Thrombocytosis in Different Stages of Cancer

Thrombocytosis	TNM Stage of Tumor			P-Value
	Stage 1 and 2 n=20	Stage 3 n=55	Stage 4 n=22	
Yes	6(30%)	17(30.9%)	8(36.4%)	
No	14(70%)	38(69.1%)	14(63.6%)	0.878

Chi-Square= 0.259

Table No. 4: Compare the Frequency of Patients with Elevated Elevated C- Reactive Protein and Platelet Count (Both) in Different Stages of Cancer

Elevated Elevated C-Reactive Protein And Platelet Count (BOTH)	TNM Stage of Tumor			P-Value
	Stage 1 and 2 n=20	Stage 3 n=55	Stage 4 n=22	
Yes	6(30%)	15(27.3%)	8(36.4%)	
No	14(70%)	40(72.7%)	14(63.6%)	0.734

Chi-Square= 0.62

Table No. 5: Compare the Frequency of Thrombocytosis and Elevated C- Reactive Protein Levels in Different Stages Of Esophageal Carcinoma For ≤ 50 Years of Age

Thrombocytosis and Elevated C-Reactive Protein Levels	TNM Stage of Tumor			P-Value
	Stage 1 and 2 n=11	Stage 3 n=39	Stage 3 n=11	
Elevated CRP	8(72.7%)	33(84.6%)	11(100%)	0.193
Thrombocytosis	6(54.5%)	13(33.3%)	3(27.3%)	0.346
Presence of both [Elevated CRP and Platelet]	6(54.5%)	11(28.2%)	3(27.3%)	0.236

There were 32(32.99%) male and 65(67.01%) female. Frequency of elevated C- reactive protein (>5 mg/dl) and platelet count (> 400,000/Liter called thrombocytosis) in esophageal carcinoma were observed in 73(75.26%) and 31(31.96%) while both were elevated in 29(29.9%) cases as presented in figure 5, 6 and 7 respectively. Elevated CRP was significantly high in stage 3 and 4 esophageal carcinoma (table 6; p=0.0005) while and platelet count (> 400,000/Liter called thrombocytosis) were not statistically significant among stages of esophageal carcinoma (table 7; p=0.878).

DISCUSSION

Cancer of the esophagus ranks as the sixth leading cause of cancer-related mortality worldwide. Notably, carcinoma of the esophagus is more prevalent in developing nations, and there exist two distinct geographical regions known as the 'Asian esophageal cancer belt.[15]. In Karachi, data reveals that it ranks as the seventh most common malignancy in men and the sixth most common malignancy in women. Interestingly, at AKUH, it is the tenth most common malignancy in men, representing 5% of cases, while at Cenar, Quetta, it emerges as the third most prevalent malignancy among men, accounting for 11% of all cancer cases.

The optimal treatment approach for advanced esophageal carcinoma remains a subject of ongoing investigation, necessitating the exploration of additional diagnostic and prognostic markers. Several biochemical markers, including carcinoembryonic antigen (CEA) and squamous cell cancer antigen (SCC-Ag), have been utilized for diagnosing and monitoring esophageal cancer patients. However, their sensitivity remains suboptimal[16]. Consequently, there is a pressing need for additional markers that can enhance the accuracy of esophageal cancer diagnosis. One such marker is a high platelet count and thrombocytosis, which are observed in some cancer patients. A higher platelet count has been inversely associated with prognosis across various cancer types, indicating that a high count is often linked with a poorer prognosis. Additionally, the elevation of preoperative serum C-reactive protein (CRP) levels has gained recognition as a reliable indicator of postoperative prognosis in patients with various malignancies, including those affecting the lung, kidney, ovary, and gastrointestinal tract. Recent research by Ibuki et al. has also highlighted the association between postoperative CRP levels and poorer overall survival and recurrence-free survival[17,18].

CONCLUSION

We conclude that elevated platelet counts may not consistently accompany the advancement of esophageal carcinoma stages. However, a substantial correlation was established between CRP levels and the TNM (Tumor, Node, Metastasis) stage in esophageal carcinoma. Notably, serum CRP concentrations were significantly elevated in patients with esophageal carcinoma. These findings underscore the potential utility of CRP as a supplementary tool for assessing tumor markers in the diagnosis of esophageal carcinoma. Given that CRP serves as a sensitive albeit nonspecific marker of inflammation, it holds promise in aiding the evaluation of esophageal carcinoma. Our study suggests that the straightforward, cost-effective, and rapid measurement of serum CRP levels may enhance the clinical diagnosis and monitoring of patients with esophageal carcinoma.

Author's Contribution:

Concept & Design of Study:	Anam Taj
Drafting:	Aisha Gul, Osama Jawed
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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