

Determination of the prognostic influence of serum inflammatory markers along with prognostic markers and their outcomes among patients with pre- and post-operative colorectal carcinoma

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ABSTRACT

Objective: To determine the prognostic influence of serum inflammatory markers along with prognostic markers and their outcomes among patients with pre- and post-operative colorectal carcinoma.

Material and methods: This cross-sectional descriptive study was done at department of Surgery, surgical unit-II, Liaquat University Hospital, Hyderabad/Jamshoro, after 06 month after the approval of synopsis. All the patient of 20-60 years of age, either gender having history of bleeding per rectum or mucous discharge, tenesmus, altered bowl habits with weight loss for ≥ 1 month duration diagnosed as colorectal cancer on histopathologic report regardless of stage & grade presented at surgical unit-II, Liaquat University Hospital Hyderabad/Jamshoro were included.

Results: A total of 112 cases were studied; their mean age was 45.16+10.52 years. Males 51.8% and females were 48.2%. The majority of the cases had abdominal pain, per rectal bleeding and weight loss and 89.3% patients had anemia. Most of the cases 84.8% had tumor location in colon and 28.6% had tumor in rectum. According to the pre-operative assessment of the inflammatory prognostic marker, WBC were raised in 59.8% of the cases, CRP was raised in 87.5% of the patients, 77.7% patients had decreased serum albumin, 61.6% had raised ESR, raised ferritin level was in 65.2% of the cases and raised LDH was in 60.7%. In accordance to the post-operative assessment of the inflammatory prognostic marker, WBC were raised in 92.9% of the cases, CRP was raised in 94.6% of the patients, 82.1% patients had decreased serum albumin, 68.8% had raised ESR, raised ferritin level was in 69.6% of the cases and raised LDH was in 73.2%. Wound infection, pneumonia, sepsis and prolonged hospital stays were the commonest complications. According to the Hospital mortality, 3.6% were died during hospital stay.

CONCLUSION: As per the study conclusion, there was significant prognostic influence of serum inflammatory markers. These markers also observed to be the significant predictors of adverse outcome among patient undergoing surgical treatment with colorectal carcinoma.

KEY WORDS: Carcinoma, colon, rectum, biomarkers, mortality

INTRODUCTION

Colorectal cancer (CRC) is the third most common cancer in males and second most common in females worldwide.¹ In developed countries the mortality rates have constantly decreased over the last years mainly due to extensive colorectal cancer screening and improved treatment options.² Yet, around 20 percent of patients with CRC present with synchronous metastasis at initial diagnosis and more than half of all CRC patients die from their disease.³ The incidence of colorectal cancer (CRC) in individuals younger than 50 years is increasing.⁴

Colorectal cancer patients present with bleeding per rectum, altered bowel habits, tenesmus, fatigue and mucus discharge and diagnosed on the basis of the history, clinical examination including digital rectal examination along with proctoscopy and colonoscopy with biopsy for histopathologic confirmation. Staging of the colorectal cancer is done by Endoscopic rectal ultrasound (ERUS), Computed tomography (CT) for chest, abdomen and pelvis, Magnetic resonance imaging (MRI) for the local disease and Positron emission tomography combined with computerized tomography (PET/CT) in case of suspected metastasis.

Evidence suggesting a role for inflammation in colorectal carcinogenesis is growing. For instance, inflammatory bowel disease, reflecting local inflammation of the colon, has been associated with an increased risk of colorectal cancer.⁵ The role of systemic inflammation in colon carcinogenesis, however, remains unclear. Chronic inflammation may initiate and promote cancer through the generation of pro-inflammatory cytokines including interleukin-6 and tumor necrosis factor and reactive oxygen species which activates transcription factors that can promote the growth of a tumor.⁶ Increases in white blood cells can also lead to a respiratory burst due to an increased uptake of oxygen, resulting in more reactive oxygen species at the site of damage and DNA damage consequently.⁷ Cancer-associated systemic inflammation is characterized by numerous alterations in many organ systems distant from the site or sites of inflammation. Activation of systemic inflammatory response in the liver results in a rapid increase in the production of acute phase proteins, such as c-reactive protein (CRP).⁸ Many disabling symptoms of cancer patients, such as fever, anemia, fatigue and loss of appetite can be attributed to the presence of systemic inflammation, and finally, metabolic changes such as loss of muscle and negative nitrogen balance manifest in cachexia, a cancer-associated wasting syndrome.⁹

Many markers of systemic inflammation are based on counts, ratios, or scores of circulating white cells or acute phase proteins as on elevated serum C - reactive protein (CRP) level and decreased serum albumin level.^{10, 11} Up to date only limited data exists to predict outcomes and survival outcome in CRC patients. Since inflammation was shown to play a crucial role in the pathogenesis and promotion of cancer progression, inflammatory biomarkers have gained more attraction as potential predictive and prognostic parameters in recent years.¹² A variety of routinely

available blood based markers of inflammation such as albumin, fibrinogen, C-reactive protein level (CRP), blood cell counts, ESR and prognostic markers includes serum ferritin, Lactate dehydrogenase (LDH) and Carcinoembryonic antigen (CEA) have been investigated in different cancer entities as prognostic tools.^{13,14} The reported prevalence for raised inflammatory markers in colorectal cancer is 24.8% respectively.¹⁵

However, the data regarding the prognosis of survival outcomes and prognostic influence in colorectal cancer is scarce in our population. Thus,

the aim of this study is to explore the value of blood-based inflammatory biomarkers as prognostic and predictive markers for outcome and survival among colorectal cancer patients and to the best of knowledge the study is the first to determine the prognostic influence of inflammatory markers and short-term survival in relation to colorectal carcinoma (CRC) in our population.

METHODS

Setting: Department of Surgery, surgical unit-II, Liaquat University Hospital, Hyderabad/Jamshoro

Duration of study: 06 month after the approval of synopsis.

Study design: Cross sectional descriptive

Sampling technique: Non probability consecutive

Sample size: The sample size is 112 patients, calculated by taking the prevalence of raised inflammatory Markers as 24.8%,¹⁵ $d = 8\%$, $n = 112$ patients with Colorectal carcinoma was.

SAMPLE SELECTION:

Inclusion criteria: The patient of 20-60 years of age, either gender having history of bleeding per rectum or mucous discharge, tenesmus, altered bowel habits with weight loss for ≥ 1 month duration diagnosed as colorectal cancer on histopathologic report regardless of stage & grade presented at surgical unit-II, Liaquat University Hospital Hyderabad/Jamshoro.

Exclusion criteria:

- Old age patient with ASA-3 and 4
- Known case of other GI malignancy, cirrhosis, and malabsorption syndrome
- Individuals already on corticosteroids, immune-suppressive therapy or on albumin therapy and antibiotic therapy.

- Known cases of chronic renal failure, nephrotic syndrome and the pregnant and lactating ladies were excluded to avoid bias.
- Vitally unstable patients due to intestinal obstruction & perforation.
- The patients already on iron supplements and recurrent blood transfusions.

DATA COLLECTION PROCEDURE: The study was conducted on the patients with colorectal cancer admitted in the surgery ward after taking informed consent. The brief clinical history was taken, relevant physical examination was performed and along with baseline investigations and the specific investigations (includes colonoscopy and biopsy, CT scan chest, abdomen and pelvis along with trans rectal ultrasound) were advised while the history of associated co-morbidities were also recorded. The patients being diagnosed as colorectal cancer regardless of stage and grade were further explored for the inflammatory markers (white blood cell count, serum albumin, erythrocyte sedimentation rate, serum C-reactive protein, fibrinogen and cytokines including interleukin-6 and tumor necrosis factor) and prognostic markers (serum LDH and ferritin), pre-operatively and post-operatively on the 3rd day and CEA level after one month by taking 2 cc venous blood sample in a 5 cc disposable syringe and send to laboratory for analysis. All the maneuvers (history taking, physical examination, sampling and data collection) was done by principal researcher while the data was collected on pre-designed proforma whereas all the financial burden of the study was paid by researcher himself. The biopsy specimen and biochemical analysis was done by senior pathologist having ≥ 5 year experience. Patient were kept in ward for 5-7 days according to the patient status and the quantity of drain and observed for in-hospital outcome. The study was performed after the approval of ethical review committee (ERC) of Liaquat University of Medical and Health Sciences - LUMHS. During the study the confidentiality were maintained and the informed consent was taken in clearly understandable national or regional (if required) languages. All basic protocols, risk and benefits of the study was discussed in detail with the patient or their attendants before their inclusion in the study and complete information regarding colorectal cancer were provided to each patient or their attendants in a separate counseling session as a part of management.

DATA ANALYSIS PROCEDURE: The data of all patients were analyzed in SPSS version 21.00. The frequency and percentage were computed for inflammatory markers and gender distribution as well as for associated co-morbidities and effect modifiers. The mean and standard deviation were calculated for quantitative variables such as age, duration, WBC, ESR and serum albumin, ferritin, LDH and CRP level. The stratification was done on outcome and to control the effect modifiers. The post stratification chi-square test was applied on categorical variables at 95% confidence interval and the p-value ≤ 0.05 was considered as statistically significant.

RESULTS

A total of 112 cases were studied; their mean age was 45.16+10.52 years, minimum 25 years and maximum 67 years. Table.1

In this study males 51.8% and females were 48.2%. Table.2

Most of the patients 53.6% were urban resident and 36.4% were rural resident. Table.3

According to the presenting complaints of the patients, the majority of the cases had abdominal pain, per rectal bleeding and weight loss, as shown in table 4.

According to the comorbidities, 67.6% of the cases had hypertension, 44.6% patients were diabetics, 49.1% of the cases were smokers, 29.5% cases were obese, 24.1% cases had dyslipidemia and most of the cases 89.3% had anemia. Table.5

In this study majority of the cases 58.0% had tumor grade T2n1m0, followed by 37.5% had tumor grade T2n0m0 and 2.7% had T1n0m0, while two patients had tumor grade T3n1m0. Table.6

According to the surgical procedures 23.2% patients underwent right hemicolectomy, 11.6% underwent left hemicolectomy, Sigmoidectomy was done in 11.6% cases, transverse colectomy was done in 11.6% of the cases, high anterior resection was done in 11.6% cases, 15.2% underwent low anterior resection and abdomino-perineal resection was done in 1.8% cases, while extended hemicolectomy was done in 13.4% of the cases. Table.7

according to tumor location most of the cases 84.8% had tumor location in colon and 28.6% had tumor in rectum. Table.8

On the patient's distribution according to surgical intent, 84.8% curative surgical intent and 15.2% palliative intent. Table.9

According to the pre-operative assessment of the inflammatory prognostic marker, WBC were raised in 59.8% of the cases, CRP was raised in 87.5% of the patients, 77.7% patients had decreased serum albumin, 61.6% had raised ESR, raised ferritin level was in 65.2% of the cases and raised LDH was in 60.7%. Table.10

In accordance to the post-operative assessment of the inflammatory prognostic marker, WBC were raised in 92.9% of the cases, CRP was raised in 94.6% of the patients, 82.1% patients had decreased serum albumin, 68.8% had raised ESR, raised ferritin level was in 69.6% of the cases and raised LDH was in 73.2%. Table.11

According to the hospital outcome, wound infection, pneumonia, sepsis and prolonged hospital stays were the commonest complications as shown in table 12.

According to the Hospital mortality, 3.6% were died during hospital stay. Table.13

Table. 1 Descriptive statistic of ag of the patients n=112

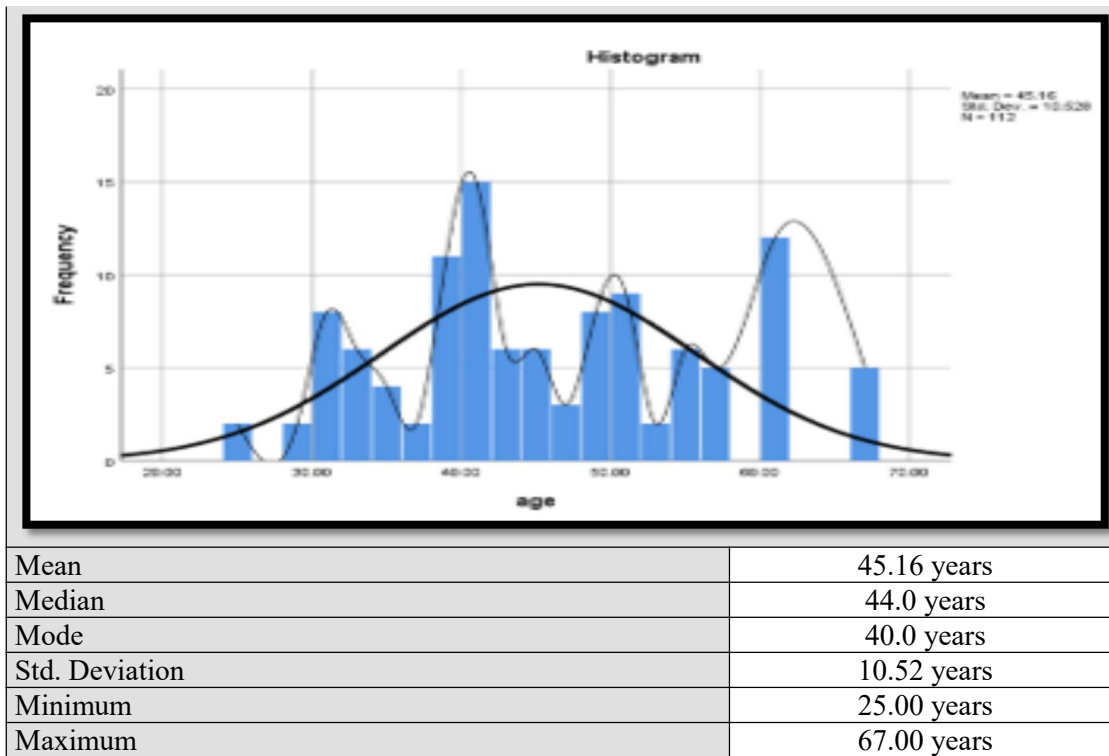


Table. 2. Patients distribution according to gender n=112

Gender	Frequency	Percent
Male	58	51.8
Female	54	48.2
Total	112	100.0

Table. 3. Patients distribution according to residence n=112

Residence	Frequency	Percent
Urban	60	53.6
Rural	52	46.4
Total	112	100.0

Table. 4. Presenting complaints of the patients n=112

Presenting complaints	Frequency	Percent
Abdominal pain	5	4.5
PR bleeding	14	12.5
12.00	5	4.5
13.00	11	9.8

16.00	8	7.1
23.00	29	25.9
34.00	3	2.7
35.00	2	1.8
37.00	2	1.8
123.00	21	18.8
137.00	12	10.7
Total	112	100.0

Table. 5. Frequency of comorbidities of the patients n=112

Comorbidities		Frequency	Percent
Hypertension	Yes	75	67.0
	No	37	33.0
Diabetes	Yes	50	44.6
	No	62	55.4
Smoking	Yes	55	49.1
	No	57	50.9
Anemia	Yes	100	89.3

Obesity	No	12	10.7
	Yes	33	29.5
Dyslipidemia	No	79	70.5
	Yes	27	24.1
	No	85	75.9

Table. 6. Patients distribution according to tumor grade n=112

Grade of tumor	Frequency	Percent
T2n0m0	42	37.5
T2n1m0	65	58.0
T1n0m0	3	2.7
T3n1m0	2	1.8
Total	112	100.0

Table. 7. Patients distribution according to surgical procedures n=112

Surgical procedures	Frequency	Percent
Right hemicolectomy	26	23.2
Left hemicolectomy	13	11.6
Sigmoidectomy	13	11.6
Transverse colectomy	13	11.6
High anterior resection	13	11.6
Low anterior resection	17	15.2
Abdomino-perineal resection	2	1.8
R extended hemicolectomy	15	13.4
Total	112	100.0

Table. 8. Patients distribution according to tumor location n=112

Tumor location	Frequency	Percent
Colon	80	71.4
Rectum	32	28.6
Total	112	100.0

Table. 9. Patients distribution according to surgical intent n=112

Surgical intent	Frequency	Percent
Curative	95	84.8
Palliative	17	15.2
Total	112	100.0

Table. 10. Pre-operative inflammatory prognostic marker of the patients
n=112

Comorbidities		Frequency	Percent
Raised WBC	Yes	67	59.8
	No	45	40.2
Raised CRP	Yes	98	87.5
	No	14	12.5
Decreased albumin	Yes	87	77.7
	No	25	22.3
Raised ESR	Yes	69	61.6
	No	43	38.4
Raised ferritin level	Yes	73	65.2
	No	39	34.8
Raised LDH	Yes	68	60.7
	No	44	39.3

Table. 11. Pre - operative inflammatory prognostic marker of the patients
 n=112

Comorbidities		Frequency	Percent
Raised WBC	Yes	104	92.9
	No	8	7.1
Raised CRP	Yes	106	94.6
	No	6	5.4
Decreased albumin	Yes	92	82.1
	No	20	17.9
Raised ESR	Yes	77	68.8
	No	35	31.3
Raised ferritin level	Yes	78	69.6
	No	34	30.4
Raised LDH	Yes	82	73.2
	No	30	26.8

Table. 12. Patients distribution according to hospital outcomes n=112

Hospital outcomes	Frequency	Percent
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Normal	34	30.4
Reoperation	8	7.1
Reopen pneumonia and prolonged hospital stay	4	3.6
Pneumonia, shock and prolonged hospital stay	2	1.8
Pneumonia, wound infection and prolonged hospital stay	8	7.1
Pneumonia	4	3.6
Sepsis, wound infection and prolonged hospital stay	14	12.5
Sepsis and prolonged hospital stay	4	3.6
Wound infection and prolonged hospital stay	11	9.8
Shock and prolonged hospital stay	2	1.8
Postoperative wound infections	21	18.8
Total	112	100.0

Table. 13. Patients distribution according to hospital mortality n=112

Mortality	Frequency	Percent
Yes	04	3.6

No	104	96.4
Total	112	100.0

DISCUSSION

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According to the hospital outcome, wound infection, pneumonia, sepsis and prolonged hospital stays were the commonest complications as shown in table 12.

According to the Hospital mortality, 7.1% were died during hospital stay. Table.13

CONCLUSION

As per the study conclusion, there was significant prognostic influence of serum inflammatory markers. These markers also observed to be the significant predictors of adverse outcome among patient undergoing surgical treatment with colorectal carcinoma. Further large-scale studies are recommended on such subject.

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