Alkaline Phosphatase: A Prognostic Biomarker in Non-Metastatic Colon Adenocarcinoma Patients - A Single-Centre Study

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ABSTRACT

Objective: To determine the prognostic significance of liver enzymes in colon carcinoma occurrence in country lifestyle and treatment follow-ups and to correlate them with tumour histopathology.

Study Design: A cross-sectional study.

Place and Duration of the Study: Department of Oncology, Karachi Institute of Radiotherapy and Nuclear Medicine, Karachi, Pakistan, from May 2023 to July 2024.

Methodology: Two hundred non-metastatic colon cancer patients with adenocarcinoma were selected from all provinces and compared with one hundred control subjects. Histopathological patients were grouped based on tumour grade and location. Treatment grouping was according to the prescribed chemotherapy FOLFOX-6 (n = 59), FOLFIRI (n = 82), and FOLFIRI + Bevacizumab (n = 59). Liver enzymes (alkaline phosphatase, alanine transaminase) and CEA colon were estimated by SPSS version 23. ANOVA was used for continuous variable comparison.

Results: Alanine transaminase (ALT) and Alkaline phosphatase (ALP) levels were significantly elevated in patients across all tumour grades before treatment ($p < 0.05$). A progressive significant decrease in ALP and carcinoembryonic antigen (CEA) levels was observed in resectable carcinoma patients on chemotherapy across all treatment groups ($p < 0.05$). FOLFOX and FOLFIRI significantly decreased ALT levels in well and moderately differentiated carcinoma patients ($p < 0.05$), whereas adding bevacizumab to FOLFIRI decreased ALT levels in poorly differentiated carcinoma patients, depending on tumour location ($p < 0.05$). ALP levels correlate with symptom duration ($p < 0.05$). Lifestyle was found associated with tumour histological grade.

Conclusion: A significant increase in ALP levels with symptom duration and decrease with treatment progress, identifies its significance as a prognostic marker in non-metastatic colon adenocarcinoma patients. Country lifestyle plays a role in colon adenocarcinoma occurrence.

Key Words: *Colonic neoplasm, Alkaline phosphatase, Bevacizumab, Prognostic marker, Alanine transaminase.*

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INTRODUCTION

Colorectal cancer (CRC) is a multifaceted disease. It is the third most commonly diagnosed malignancy and the second leading cause of cancer-related deaths worldwide. Adenocarcinomas derived from colorectal mucosal epithelial cells account for more than 90% of all colorectal carcinomas.[1]

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A higher incidence of CRC was reported in young to middle age groups with a decreased incidence in older age, this burden will increase till 2030 in the USA.[2] Jiang *et al*. reported that raised alkaline phosphate (ALP) levels have been associated with poor prognosis in patients with colorectal cancer. Tumour can cause overproduction of ALP which then leaks into the bloodstream.[3] Increased ALP levels as compared to carcinoembryonic antigen (CEA) reported to have more significant importance in early disease diagnosis and treatment progress. CEA does not emerge as a specific marker of colon cancer, since it may also be increased in certain non-malignant conditions such as smoking and inflammatory bowel disease.[4] Alkaline phosphatase appears to be an important prognostic marker, hence present study was designed to measure alanine transaminase (ALT) and ALP levels along with CEA in histopathologically graded patients at disease diagnosis and during treatment progress.

The first-line treatment suggested by studies was FOLFOX (5-flourouracil, oxaliplatin) and FOLFIRI (Irinotecan), and the second-line treatment included angiogenesis inhibitor (bevacizumab).[5] FOLFOX inhibits DNA synthesis in cancer cells, and Irinotecan inhibits DNA replication.

Unhealthy lifestyle as a colon cancer cause presented in the past include, unhealthy lifestyle, increased BMI, and poor dietary habits.[6] The present study was targeted to identify the risk factors of colon carcinoma occurrence in the present lifestyle of Pakistan and also to investigate the role of ALP in disease diagnosis and treatment prognosis.

METHODOLOGY

This cross sectional study was conducted from May 2023 to July 2024 on 200 newly diagnosed colon adenocarcinoma patients without any prior treatment, selected from the oncology outpatient Karachi Institute of Radiotherapy and Nuclear Medicine, Karachi, Pakistan, which receives patients from all over Pakistan. Both male and female patients with stage II and III adenocarcinoma were included in the study. Patients selected were non-smokers. Data of 200 patients had primary colon carcinoma. Patients who were under 18 years, had metastasis, suffering from comorbidities, and smokers were excluded from the study. Data of 200 patients were collected after receiving the ethical approval from KIRAN Hospital and Hamdard College of Medicine and Dentistry, Karachi, Pakistan (No: HCMD/183/2023).

Carcinomas were confirmed through biopsy. Adenocarcinoma of the colon was selected due to the availability of large patient population. The control group included healthy individuals of both genders belonging to the same geographical area as patients. The questionnaire recorded health status, medical history, known or suspected risk factors for cancer, age, occupation, and lifestyle. Patients gave verbal agreement for a face-to-face interview, and they were provided with details about the relevance of the conducting research during the interview.

The body mass index (BMI) of patients as well as controls was determined using baseline height and weight represented in kg/m^2. It was calculated as Weight (Kg)/[(Height ($metre^2$)]. Physical activities were assessed using the WHO criteria, with a minimum of 30 minutes of moderate activity five times per week, in addition to regular routines. Physical activity types included walking and cycling. Fibre intake of less than 100 grams was considered negligible. Red meat intake was defined as 500 grams three times a week. The term *DHABA* food was explained as a roadside small hotel with sub-standard and unhygienic food. Wood cooking was also considered as a risk factor and at least two hours daily wood cooking was considered as standard for patient inclusion.

A sample size of a minimum of 162 participants across 3 treatment groups was determined for comparisons using repeated measures ANOVA. This calculation was based on a predicted effect size (f) of 0.25, a probability of Type I error of 0.05, and a power of 0.95, considering a total of 3 comparison groups with 3 repeated measures, correlation among repeated measures = 0.5, and non-sphericity correction = 1. The G Power 3.1.9.4 software was employed for this calculation. Over the course of this project which satisfies the calculated minimum number of patients needed to observe a clinically significant effect.

The software SPSS version 23 was used to analyse data. All results were expressed as frequencies and percentages for categorical variables such as gender and age, mean ± SEM for continuous variables such as BMI and level of ALT, ALP, and CEA. First, the Kolmogorov-Smirnov test was used to test the normality assumption for each variable. Dual comparisons between groups were analysed using the Chi-square test for categorical variables and independent samples t-test for continuous variables. ANOVA was used for comparisons between more than three variables. The homogeneity of variance was tested using Levene's test. Paired sample t-test was used to assess significant difference between before *versus* treatment cycles and to test whether medicines interacted with variations of ALT, ALP, and CEA. The results were considered to be statistically significant at $p < 0.05$.

Tissue sampling and histopathological evaluation techniques used were in accordance with the methods published by Slaoui *et al*.[7] Colon cancer was classified as based on AJCC.[8,9] The treatment was as per the NCCN Guidelines version 3.2023 pMMR/MSS colon cancer[10] based on colon cancer stage, stage II or III CRC patients were included for study. The procedure identified high-risk features for cancer staging as histological grade, significant lymph vascular or perineural invasion, and mucinous component.

The treatment pattern followed was first surgery followed by chemotherapy; the chemotherapy selected was modified FOLFOX - (mFOLFOX-6),[11] FOLFIRI + BEVACIZUMAB,[12] and FOLFIRI.[13] Twelve (12) cycles post-surgery of each medicine were given at the interval of two weeks. Blood sample collection for liver enzyme and CEA estimation and prognosis follow-up was done three times. The first time was when the patient visited OPD after biopsy confirmation without any treatment, second time was post-surgery with 6 cycles of chemotherapy, and finally after complete treatment with 12 chemotherapy cycles. Treatment response was measured by evaluating CEA, ALT, and AST values.

ALT was estimated by the International Federation of Clinical Chemistry (IFCC) recommended standardised methods for the determination of ALT.[14] The method described here is derived from the IFCC reference method. The assay method for ALP is standardised against IFCC.[15] CEA colon estimation was performed on LIAISON analyzer family-314311.[16]

RESULTS

Out of the total 200 patients with colon adenocarcinoma and 100 control subjects, the majority 156 (78%) were male patients. Sixty-eight percent male patients were aged between 41 and 60 years. Gender, age, and BMI were found to be highly significant in colon cancer patients as compared to the control group (Table I).

Table I: Demography-wise distribution of control subject and colon cancer patient.

Variable	Control (n = 100)	Colon cancer patient (n = 200)	p-value
Gender			
Male	50 (50%)	156 (78%)	<0.001
Female	50 (50%)	44 (22%)	
Age			
≤40 years	17 (17.0%)	2 (1%)	
41-60 years	64 (64.0%)	136 (68%)	<0.001
≥61 years	19 (19.0%)	62 (31%)	
Body mass index (BMI)	22.64 ± 0.62	30.10 ± 0.08	<0.001

**p-values were determined using Chi-square for gender and age and independent sample t-test for BMI.*

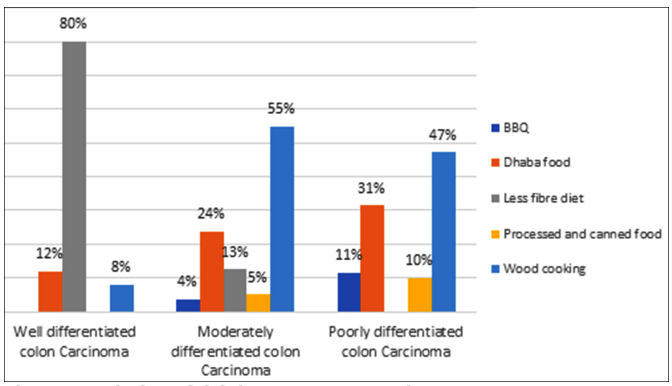

Figure 1: Relation of risk factor tumour grade.

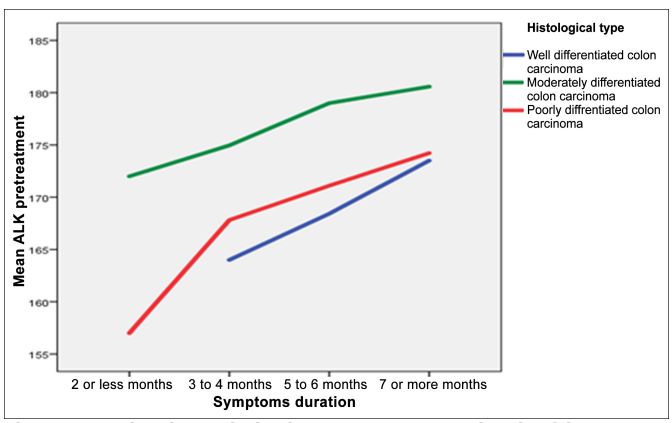

Figure 2: Grade-wise variation in pretreatment ALP levels with symptom duration.

Figure 1 shows the relation between histological grade and risk factors. For well-differentiated carcinoma, less fibre diet is the main risk factor whereas for moderately and poorly differentiated carcinoma, wood cooking was found to be the main contributing factor followed by the consumption of '*Dhaba*' (roadside stalls) food.

Post-surgery chemotherapy treatment response in resectable colon carcinoma patients was analysed. The chemotherapy type included was modified FOLFOX-6, FOLFIRI, and FOLFIRI- added bevacizumab. ALT and ALP levels were significantly high in patients with all tumour grades as compared to pre-treatment levels ($p < 0.05$).

Post-surgery treatment with six cycles of FOLFOX and FOLFIRI significantly decreased ALT levels in well and moderately differentiated carcinoma patients ($p < 0.05$). Twelve-cycle treatment resulted in a greater decrease in ALT levels compared to the 6-cycle treatment ($p < 0.05$). In poorly differentiated carcinoma patients, no significant change in ALT levels was observed between six and 12 cycles. The addition of bevacizumab to post-surgery FOLFIRI significantly decreased ALT levels in moderately-differentiated carcinoma patients and in the right-sided colon of poorly- differentiated carcinoma patients.

Post-surgery chemotherapy with modified FOLFOX-6, FOLFIRI, and FOLFIRI added bevacizumab significantly decreased ALP and CEA levels in well, moderately, and poorly differentiated carcinoma patients after six cycles as compared to pre-treatment levels ($p < 0.05$). Additionally, a significant decrease in ALP levels ($p < 0.05$) was observed after 12 cycles compared to six cycles (Table II).

Non-significant variations in ALP and CEA levels with symptom duration in colon carcinoma patients were observed. In moderately-differentiated carcinoma patients, ALP and CEA levels did not vary in the first two months after symptom appearance. Increases in ALP and CEA levels with symptom duration after two months were first analysed in left-side moderately and poorly differentiated carcinoma patients. In left-sided colon moderately differentiated carcinoma patients, ALP levels variations with symptom duration were significant ($p < 0.05$). In right-sided colon poorly differentiated carcinoma patients, CEA level variations with symptom duration were significant ($p < 0.05$, Table III).

Figure 2 shows that as the symptom's duration increases, the mean level of ALP before treatment slightly increases in well, moderate, and poorly differentiated carcinoma. The level of ALP was high in moderately differentiated carcinoma patients.

DISCUSSION

The study aimed to identify modifiable and non-modifiable risk factors for the incidence of non-metastatic colon carcinoma occurrence among patients in one of the hospitals of Karachi treating cancer patients as well as to investigate a cost-effective and readily accessible prognostic marker for earlier disease diagnosis and improved treatment outcomes. Adenocarcinoma was chosen, owing to its high prevalence in the country. A study was conducted on patients from several regions of Pakistan including Sindh, Punjab, Khyber Pakhtunkhwa, and Balochistan, attending the cancer outpatient department in Karachi.

Demographic variables and lifestyle factors of any country significantly influence disease occurrence. The results of this study reported majority of male and female patients (n = 136) with the disease were aged 41-60 years followed by those in the advanced-age category. The study indicated a significant proportion (156) of male patients. The disparity in disease occurrence across genders necessitates additional investigation; nevertheless, it may be linked to obesity and elevated BMI in both males and females[17] as BMI influences inflammation and the rise of pro-inflammatory cytokines.[18] The BMI of cancer patients in the present study was significantly elevated compared to that of control subjects.

Table II: Grade-wise variations in ALP, AST, and CEA colon levels with treatment plan included post-surgery with 12 cycles of chemotherapy-modified FOLFOX-6, FOLFIRI, and FOLFIRI

Subject	Alanine transaminase (U/L)			Alkaline phosphatase (U/L)			CEA Colon (ng/ml)		
	Before treatment	Post-surgery +6 cycles	Post-surgery +12 cycles	Before treatment	Post-surgery +6 cycles	Post-surgery +12 cycles	Before treatment	Post-surgery +6 cycles	Post-surgery +12 cycles
Control	**23.78 ± 0.85**			**67.8 ± 1.88**			-		
Modified FOLFOX-6 (n = 59)									
Well-differentiated colon carcinoma (n = 24)									
RT. Side colon (n = 14)	46.21 ± 1.15[c]	37.57 ± 2.01[a]	29.36 ± 1.21[b]	167.0 ± 1.75[c]	139.43 ± 4.62[a]	87.50 ± 4.85[b]	11.14 ± 0.47	10.04 ± 0.42[a]	7.42 ± 0.27[b]
LT. Side colon (n = 10)	46.30 ± 2.62[c]	37.70 ± 1.97	28.90 ± 1.68[b]	167.10 ± 2.08[c]	146.20 ± 2.94[a]	89.30 ± 2.07[b]	12.63 ± 0.40[d]	11.46 ± 0.33[a,d]	9.88 ± 0.37[b,d]
Moderately-differentiated colon carcinoma (n = 21)									
RT. Side colon (n = 0)	-	-	-	-	-	-	-	-	-
LT. Side colon (n = 21)	49.71 ± 1.01[c]	38.81 ± 1.11[a]	29.43 ± 1.17[b]	176.81 ± 1.52[c]	146.19 ± 1.93[a]	84.48 ± 0.98[b]	15.01 ± 0.21	12.59 ± 0.25[a]	10.99 ± 0.24[b]
Poorly-differentiated colon carcinoma (n = 14)									
RT. Side colon (n = 0)	-	-	-	-	-	-	-	-	-
LT. Side colon (n = 14)	46.07 ± 0.95[c]	39.86 ± 1.74[a]	39.36 ± 1.66	169.86 ± 1.66[c, d]	144.0 ± 1.99[a]	117.79 ± 1.90[b,d]	18.85 ± 0.79[d]	16.47 ± 0.76[a,d]	12.64 ± 0.34[b,d]
FOLFIRI (82)									
Well-differentiated colon carcinoma (n = 23)									
RT. Side colon (n = 8)	46.50 ± 1.43[c]	37.25 ± 1.80[a]	29.0 ± 0.63[b]	168.25 ± 2.14[c]	147.63 ± 2.57[a]	88.50 ± 1.31[b]	11.80 ± 0.66	10.67 ± 0.76[a]	8.11 ± 0.65[b]
LT. Side colon (n = 15)	45.0 ± 1.78[c]	40.47 ± 1.08[a]	28.73 ± 0.73[b]	164.67 ± 1.65[c]	143.67 ± 2.23[a]	91.20 ± 2.17[b]	13.25 ± 0.37	11.98 ± 0.35[a]	10.16 ± 0.31[b,d]
Moderately-differentiated colon carcinoma (n = 33)									
RT. Side colon (n = 12)	46.50 ± 1.16[c]	43.50 ± 1.56	31.67 ± 0.92[b]	174.67 ± 2.08[c]	146.08 ± 3.06[a]	84.03 ± 1.52[b]	14.65 ± 0.26	13.27 ± 0.28[a]	11.35 ± 0.25[b]
LT. Side colon (n = 21)	50.10 ± 0.99[c,d]	38.43 ± 1.09[a, d]	26.05 ± 0.83 [b, d]	179.19 ± 1.74[c]	147.0 ± 1.78[a]	86.71 ± 1.68[b]	15.04 ± 0.21	13.39 ± 0.27[a]	11.16 ± 0.36[b]
Poorly-differentiated colon carcinoma (n = 26)									
RT. Side colon (n = 7)	49.14 ± 2.31[c]	41.86 ± 2.34	39.57 ± 2.74	170. 43 ± 2.36[c]	158.0 ± 0.82[a]	123.0 ± 0.82[b]	19.11 ± 0.34	16.69 ± 0.35[a]	13.40 ± 0.36[b]
LT. Side colon (n = 19)	44.63 ± 1.12[c]	37.95 ± 1.92[a]	40.95 ± 1.22	168.26 ± 1.52[c]	144.53 ± 1.47[d]	117.58 ± 1.84[b]	19.07 ± 0.43	16.73 ± 0.54[a]	13.73 ± 0.50[b]
FOLFIRI + Bevacizumab (n = 59)									
Well-differentiated colon carcinoma (n = 3)									
RT. Side colon (n = 3)	45.67 ± 4.33[c]	38.33 ± 3.28	31.0 ± 1.53	166.33 ± 4.98[c]	142.67 ± 8.97[a]	86.0 ± 3.21[b]	12.87 ± 0.61	11.60 ± 0.31	10.43 ± 0.37
LT. Side colon (n = 0)	-	-	-	-	-	-	-	-	-
Moderately-differentiated colon carcinoma (n = 26)									
RT. Side colon (n = 11)	45.55 ± 1.31[c]	43.18 ± 0.83	30.18 ± 0.99[b]	178.36 ± 1.97[c]	143.73 ± 2.59[a]	84.55 ± 1.04[b]	13.87 ± 0.29	12.86 ± 0.26[a]	10.94 ± 0.19[b]
LT. Side colon (n = 15)	48.40 ± 0.92[c]	37.80 ± 1.32[a,d]	24.33 ± 1.05[b,d]	179.47 ± 1.82[c]	142.07 ± 3.02[a]	85.06 ± 1.23[b]	15.28 ± 0.22[d]	14.03 ± 0.31[a,d]	11.63 ± 0.36[b]
Poorly-differentiated colon carcinoma (n = 30)									
RT. Side colon (n = 12)	46.33 ± 1.53[c]	38.58 ± 1.96[a]	27.92 ± 1.67[b]	171.83 ± 1.47[c]	148.50 ± 1.04[a]	113.50 ± 1.04[b]	16.42 ± 0.48	14.76 ± 0.21[a]	12.18 ± 0.33[b]
LT. Side colon (n = 18)	44.06 ± 2.42[c]	37.33 ± 2.32	38.28 ± 1.16[d]	168.06 ± 1.78[c]	144.83 ± 1.63[a]	120.39 ± 1.56[b,d]	18.58 ± 0.51[d]	16.48 ± 0.58[a,d]	13.42 ± 0.46[b]

(p <0.05) [a]Statistically significant between pre-treatment and post-surgery +6 cycle treatment. [b]Statistically significant between post-surgery +6 cycle treatment and post-surgery +12 cycle treatment. [c]Statistically significant between control and grade-wise variation in colon cancer before treatment [d]Statistically significant between RT. Side colon and LT. Side colon. Paired sample t-test was used to determine the significant difference between before-treatment and post-surgery +6 cycle and post-surgery +6 cycle treatment and post-surgery +12 cycle. Statistically significant between control and grade-wise variation and RT. Side colon and LT. Side colons were determined by independent sample t-test.

Table III: Grade-wise variation between symptoms duration with alkaline phosphatase (U/L) and CEA colon (ng/ml) pre-treatment.

Symptoms duration	Grade-wise variation ALP levels (U/L)						Grade-wise variation in CEA levels (ng/ml)					
	Well-differentiated colon carcinoma (n = 50)		Moderately-differentiated colon carcinoma (n = 80)		Poorly-differentiated colon carcinoma (n = 70)		Well-differentiated colon carcinoma (n = 50)		Moderately-differentiated colon carcinoma (n = 80)		Poorly-differentiated colon carcinoma (n = 70)	
	RT. side colon (n = 25)	LT. side colon (n = 25)	RT. side colon (n = 23)	LT. side colon (n = 57)	RT. side colon (n = 19)	LT. side colon (n = 51)	RT. side colon (n = 25)	LT. side colon (n = 25)	RT. side colon (n = 23)	LT. side colon (n = 57)	RT. side colon (n = 19)	LT. side colon (n = 51)
≤2 months	-			183.00 ± 2.83		157.00 ± 0.00	-	-	-	15.65 ± 0.65	-	17.20 ± 0.00
3 to 4 months	168.75 ± 6.24	163.67 ± 8.96	182.0 ± 1.41	175.24 ± 7.00	167.50 ± 0.71	168.29 ± 5.62	9.87 ± 0.76	12.73 ± 0.64	14.05 ± 0.75	15.15 ± 0.17	20.20 ± 0.10	19.76 ± 1.59
5 to 6 months	167.00 ±6.93	166.25 ± 6.08	176.18 ± 8.30	180.96 ± 6.61	171.23 ± 6.17	168.94 ± 7.06	11.84 ± 0.41	13.04 ± 0.39	14.33 ± 0.31	15.07 ± 0.22	16.81 ± 0.47	18.97 ± 2.31
≥7 months	167.25 ± 5.12	165.00 ± 7.24	175.60 ± 5.93	177.56 ± 8.38	173.50 ± 2.65	169.21 ± 7.21	12.05 ± 0.83	13.02 ± 0.50	14.27 ± 0.33	14.90 ± 0.29	17.97 ± 0.99	18.13 ± 2.53
p-value	0.893	0.799	0.513	0.045[a]	0.463	0.375	0.109	0.943	0.941	0.766	0.048*	0.191

(p <0.05).Significant in moderately differentiated left-sided colon.Significant in the poorly differentiated right-side colon.

The objective of the present study was also to assess the influence of modifiable risk factors associated with the incidence of colon carcinoma. The environmental conditions and lifestyle of a country significantly influence the prevalence of specific diseases.

The lifestyle, including dietary habits of any country, evolves with time and is influenced by available resources, literacy rate, and economic capacity. In recent years, the use of wood for cooking has risen in the country due to gas scarcity, leading to an increased occurrence of moderately-differentiated and poorly-differentiated adenocarcinoma colon. As illustrated in the results, present findings are corroborated by the mechanisms outlined in the past studies. A mechanism elucidates the hypothesis that cooking with wood, charcoal, and dung leads to exposure to organic carcinogens, heterocyclic amines, and polycyclic aromatic hydrocarbons.[19] This study also illustrated that a diet lacking in fibres and an adequate intake of fruits, vegetables, and wheat bran is a contributing cause to the elevated incidence of well-differentiated carcinoma in Pakistan.

The significance of dietary fibre should not be overlooked; Whole grains, fruits, and vegetables mitigate the risk of obesity and diabetes, which are significant contributors to the incidence of colon carcinoma. Fibre enhances stool bulk and reduces stool transit duration, both of which confer a preventive effect against the incidence of colon carcinoma. Vitamins found in fruits and vegetables have antioxidant properties and contribute to the prevention of colon carcinoma.[20]

The liver's function in the manifestation of diseases, including cancer, cannot be overlooked. The patients examined were non-metastatic to distant organs at the time of illness manifestation. The study aimed to investigate the liver enzymes ALP and ALT as well as CEA, to identify an inexpensive and readily accessible prognostic marker for early illness detection and to monitor therapy efficacy.

According to previous studies, increased ALP levels as compared to CEA have more significant importance in early disease diagnosis and treatment progress. CEA does not emerge as a specific marker of colon cancer, since it may also be increased in certain non-malignant conditions such as smoking, alcoholism, and inflammatory bowel disease,[4] however, the diagnostic tool was not established for non-metastatic patients. The importance of CEA is indisputable, nevertheless, its availability and affordability across Pakistan constrain its relevance. The cost of each test for CEA is PKR

3000 to 4000, which is unaffordable for the lower class and, its availability is restricted to urban areas. Conversely, ALP is readily available nationwide at a lower cost of PKR 650 to 800.

This study significantly indicated the elevated ALT and ALP levels in non-metastatic cancer patients across all tumour grades compared to control subjects. Control levels of ALP varied from 60 to 80 U/L, while ALT levels ranged from 17 to 36 U/L. Previous research indicated an inverse relationship between ALT levels and the incidence of carcinoma.[21] The current study indicated elevated ALT levels during the onset of symptoms, so contradicting previous research and undermining its assessment as a prognostic marker. Elevated ALP levels can be attributed to inflammation caused by obesity resulting from fat build-up. A lipid-rich meal induces the release of this enzyme into the intestinal lymphatics, leading to a 20% rise in total plasma ALP activity 28. The study already demonstrated that the BMI of cancer patients is significantly elevated compared to control participants; thus, in non-metastatic situations, one contributing reason to higher ALP levels may be BMI.

Post-resection chemotherapy was administered using the regimens, modified FOLFOX-6, FOLFIRI, and FOLFIRI with the addition of bevacizumab. The therapeutic response was assessed by the notable reduction in liver enzymes and CEA levels with treatment progress. A total of 59 patients received modified FOLFOX whereas 82 individuals were administrated FOLFIRI; a substantial reduction in ALP and CEA levels across all tumour grades was seen ($p < 0.05$). The reduction in ALT levels was related to tumour grade, location, and dosage. Previous research corroborates the present study's findings, indicating that survival benefits do not vary based on the medication regimen employed for therapy; nonetheless, FOLFOX is favoured due to its cost-effectiveness and favourable toxicity profile.[22] Treatment was administered to 59 patients using FOLFIRI in conjunction with bevacizumab. ALP levels markedly decreased across all tumour grades, in both right and left colon, however, the reductions in ALT and CEA levels were specific to tumour grade and location, as shown in the results.

The current study correlated the levels of ALP and CEA with the duration of symptom onset before treatment. This aspect was distinctive to the study, revealing that both markers were not significantly raised in the initial two months of symptom duration. Significantly raised ALP levels in the left colon of moderately-differentiated carcinoma and CEA levels in the right colon of poorly-differentiated carcinoma were analysed. This study also illustrated considerably-elevated ALP levels in patients with moderately-differentiated colon carcinoma. This may be substantiated by previous research that linked elevated ALP levels to an increase in tumour burden.[3] One of the limitations of this study was that the samples were obtained from a single centre, which impacted the generalisability of the findings. A multi-centre study would have offered a more extensive foundation for comparison. Additionally, due to the low availability of other forms of colon cancer, only adeno-carcinoma was included in this investi-gation.

CONCLUSION

The study highlights that ALP serves as a superior prognostic marker for diagnosis and treatment progress monitoring, regardless of tumour grade and location. Assessing availability within the country and estimating costs further enhances its predictive significance. Furthermore, the use of a low-fibre diet and wood for cooking are probable factors causing colon cancer in Pakistan.

ETHICAL APPROVAL:
Ethical approval was obtained from the Ethical Review Committee on March 7, 2023 (Ref. No: HCMD/183/2023).

PATIENTS' CONSENT:
Verbal consent was obtained from each patient, with assurance of name anonymity, following approval from the Head of Clinical Oncology at KIRAN Hospital, Karachi.

COMPETING INTEREST:
The authors declare no competing interests, financial or otherwise, that could influence the content, methodology, or interpretation of this article. There are no personal, professional, or financial relationships that could potentially bias the research or its findings.

AUTHORS' CONTRIBUTION:
AS: Conceptualisation, literature review, data curation, formal analysis, write-up, critical review, and editing.
SAM: Literature review, data curation, writing of the original draft, and editing.
UR: Literature search, methodology, data analysis, writing of the original draft, editing, and proofreading.
MRA: Literature search, drafting, editing, and proofreading.
FR: Critical review and feedback, proofreading, and critical feedback.
UB: Data Curation, formal data analysis and results, review and editing.
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