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Frequency and Clinical Correlates of Hypoalbuminemia in Colorectal Cancer Patients at A Tertiary Care Hospital

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ABSTRACT

Colorectal cancer is often associated with hypoalbuminemia, a marker of poor nutritional status and systemic inflammation. Low albumin levels in colorectal cancer patients are linked to worse outcomes, including higher morbidity and mortality. **Objectives:** To assess the frequency of hypoalbuminemia and its association with clinical and biochemical variables among colorectal cancer patients at Liaquat University Hospital, Hyderabad. **Methods:** This cross-sectional study was conducted from January 14, 2022, to July 13, 2022, at the Department of Surgery, Liaquat University Hospital, Hyderabad. 124 patients who were diagnosed with colorectal cancer aged between 20 to 60 years and of either gender were included in the study. Colorectal cancer was confirmed histopathologically. Patients with other gastrointestinal malignancies, chronic liver diseases, nephrotic syndrome, and those on corticosteroid or immune-suppressive therapy were excluded from the study. **Results:** The study identified the presence of hypoalbuminemia in n=73 (58.9%) of the patients. Among them, 38 (52.1%) were classified as obese (≥30.0), with a p-value of 0.001. The mean duration of the disease was found to be 49.2 ± 7.10 weeks, which also showed a significant correlation (p=0.01). Additionally, elevated C-reactive protein levels and erythrocyte sedimentation rates showed a strong association with hypoalbuminemia (p=0.001). Hypocalcaemia (34.2%) and hypomagnesemia (27.4%), were significantly associated with hypoalbuminemia. **Conclusions:** It was concluded that hypoalbuminemia is a prevalent and clinically significant condition among colorectal cancer patients. The high prevalence of hypoalbuminemia is strongly associated with obesity, longer disease duration, rural residency, elevated inflammatory markers,and electrolyte imbalances (hypocalcaemia, hypomagnesemia).

INTRODUCTION

Colorectal cancer (CRC) is one of the leading causes of cancer-related morbidity and mortality worldwide [1]. Accounting for a significant disease burden, CRC ranks among the most common cancers globally, affecting millions of individuals each year [2]. In recent decades, the global incidence of CRC has increased, particularly in developed countries, largely due to ageing populations and lifestyle changes such as diet, smoking, and decreased physical activity. Sedentary behaviours, high consumption of red and processed meats, low fiber intake, and obesity have been well-documented as risk factors contributing to this rise. Concurrently, improved diagnostic tools and awareness campaigns in developed nations have also led to earlier detection and an apparent rise in incidence rates [3]. In Pakistan, CRC has become increasingly prevalent, with cases primarily affecting individuals over 50 years of age, despite the country being historically considered a low-risk region for this malignancy [4]. The shift may be attributed to urbanization, dietary transitions, and inadequate screening practices. Unlike developed countries, where screening programs have been systematically implemented, the lack of such initiatives in Pakistan contributes to delayed diagnoses and a higher proportion of advanced-stage presentations. Additionally, sociocultural factors and limited healthcare access further exacerbate the burden of CRC in the region [5]. CRC is

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frequently associated with systemic complications, among which hypoalbuminemia stands out as an important prognostic marker. Albumin, a protein produced in the liver, is a major contributor to maintaining plasma oncotic pressure and transporting molecules such as hormones, fatty acids, and drugs [6]. Traditionally, serum albumin levels have been used to assess nutritional status, but in cancer patients, hypoalbuminemia is often linked to more complex factors, such as systemic inflammation and tumor burden [7]. Systemic inflammation in cancer, driven by cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), disrupts albumin synthesis and contributes to increased protein catabolism. Tumor-related cachexia, another hallmark of advanced cancer, also plays a key role in hypoalbuminemia [8]. Hypoalbuminemia has profound clinical implications for CRC patients. Some studies have reported that hypoalbuminemia occurs in up to 60% of patients with CRC [9], and is associated with poor prognosis, including increased postoperative complications, prolonged hospitalization, and mortality [10]. Furthermore, hypoalbuminemia often reflects a combination of malnutrition, disease progression, and inflammatory responses, making it a valuable marker for assessing overall patient health and predicting outcomes. In surgical CRC patients, low preoperative albumin levels are linked to delayed wound healing, infections, and an elevated risk of morbidity and mortality, highlighting the need for early identification and intervention [11]. In low- and middle-income countries like Pakistan, the management of hypoalbuminemia in CRC is particularly challenging due to limited access to nutritional support and palliative care. Despite its clinical importance, hypoalbuminemia remains an under-recognized issue in resource-constrained settings, further emphasizing the need for comprehensive care strategies.

The study aims to assess the frequency of hypo-albuminemia in patients with CRC at the University Hospital and to investigate the association of hypo-albuminemia with various demographic and clinical factors such as disease stage, comorbidities and inflammatory markers between different types

METHODS

This cross-sectional study was conducted over from January 14, 2022, to July 13, 2022, at the Department of Surgery, Liaquat University Hospital, Hyderabad. 124 patients who were diagnosed with colorectal cancer aged 20-60 years and of either gender were included in the study. Colorectal cancer was confirmed histopathologically. The inclusion criteria focused on adult patients within this age range to minimize the impact of extreme age-related variables on hypoalbuminemia and to align with the typical age range for CRC onset in Pakistan. Patients with other gastrointestinal malignancies, chronic liver diseases, nephrotic syndrome, and those on corticosteroid or immune-suppressive therapy were excluded to eliminate confounding factors that independently contribute to hypoalbuminemia and systemic inflammation. The sample size was calculated via WHO Open Epi software by taking the prevalence of hypoalbuminemia in Colorectal Cancer Patients as 8.85% with a 5% margin of error and 95% confidence interval [12]. Informed consent was taken. The study was approved by the Ethical Review Committee of Liaquat University of Medical & Health Sciences, Jamshoro vide letter No. LUMHS/REC/-110; dated. CRC diagnosis was confirmed histopathologically through biopsies obtained during colonoscopy or surgical procedures. The staging of CRC was conducted using the tumor/node/metastasis (TNM) classification system, developed by the American Joint Committee on Cancer (AJCC) [13]. This TNM classification system evaluates tumor size (T), regional lymph node involvement (N), and distant metastasis (M), providing a comprehensive assessment of disease progression. Demographic data, clinical history, and laboratory results were recorded for each patient. Serum albumin levels were measured using venous blood samples collected under standardized fasting conditions. CRP levels were quantified using a high-sensitivity immune-turbid-metric assay. Hypoalbuminemia was defined as serum albumin levels <3.5 g/dL, based on standard clinical thresholds for malnutrition and inflammation. Additional parameters included body mass index (BMI), C-reactive protein (CRP) levels, serum creatinine, serum calcium, magnesium and serum bilirubin, erythrocyte sedimentation rate (ESR), and comorbidities such as hypertension, diabetes mellitus, and smoking status. Quality controls and standard calibration protocols for all laboratory parameters were implemented to ensure the reliability and reproducibility of results. Duration of disease was also noted, and the relationship between these variables and hypoalbuminemia was analyzed. Data analysis was performed using SPSS version 22.0. Frequencies and percentages were calculated for categorical variables, while means and standard deviations were calculated for continuous variables. The chi-square test was used to assess the significance of the association between hypoalbuminemia and the other variables of interest. A p-value≤0.05 was considered statistically significant.

RESULTS

Among 124 patients, the mean age was 57.83 ± 8.65 years, with a slightly higher proportion of male (54%) than female (46%). The majority (61.3%) were from rural areas, and nearly half (46%) were classified as obese (BMI≥30.0).

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Notably, 52.4% had diabetes mellitus, 37.9% had hypertension, and 36.3% were smokers. Biochemically, inflammatory markers were elevated in a significant portion of patients, with 54% showing elevated CRP and 58.1% elevated ESR. Hypoalbuminemia was also linked with low calcium levels (25%) and low magnesium levels (20.2%). Elevated bilirubin and creatinine levels were observed in 34.7% and 13.7% of patients, respectively (Table 1).

Table 1: Demographics and Clinical Characteristics of Colorectal Cancer Patients (n=124)

Characteristics	Value
Mean Age (years)	57.83 ± 8.65
Gender	
Male	67 (54%)
Female	57 (46%)
Residential Area	
Rural	76 (61.3%)
Urban	48 (38.7%)
BMI Category	
Underweight (<18.5)	8 (6.5%)
Normal weight (18.5–24.9)	32 (25.8%)
Overweight (25.0–29.9)	27 (21.0%)
Obesity (≥30.0)	57 (46.0%)
Mean Duration of Disease (weeks)	48.62 ± 7.93
Comorbidities	
Hypertension	47 (37.9%)
Smoking	45 (36.3%)
Diabetes Mellitus	65 (52.4%)
Biochemical Profile	
Elevated CRP	67 (54.0%)
Elevated ESR	72 (58.1%)
Raised Creatinine	17 (13.7%)
Raised Bilirubin	43 (34.7%)
Hypocalcemia	31 (25.0%)
Hypomagnesemia	25 (20.2%)

The frequency of hypoalbuminemia in colorectal cancer patients was found to be 58.9% (n=73). A comparison of the patients with and without hypoalbuminemia revealed that patients with hypoalbuminemia had a slightly higher mean age (58.2 years) compared to those without (56.1 years). A larger proportion of rural residents (67.1%) exhibited hypoalbuminemia compared to urban patients (32.9%). Obesity (BMI ≥30.0) was significantly more common in hypoalbuminemia patients (52.1%) versus those without (15.7%), and they also had a longer mean disease duration (49.2 vs. 37.2 weeks). In terms of clinical markers, hypoalbuminemia was strongly associated with elevated CRP (76.7% vs. 21.6%) and ESR (83.6% vs. 21.6%). Biochemical disturbances, such as hypocalcaemia and hypomagnesemia, were also more prevalent in hypoalbuminemia patients (Table 2).

Table 2: Hypoalbuminemia Distribution in Associated Factors

Characteristics	Hypoalbuminemia Present (n=73)	Hypoalbuminemia Absent (n=51)
Mean Age (years)	58.2 ± 8.45	56.1 ± 8.80
Gender		
Male	39 (53.4%)	28 (54.9%)
Female	34 (46.6%)	23 (45.1%)
Residential Area		
Rural	49 (67.1%)	27 (52.9%)
Urban	24 (32.9%)	24 (47.1%)
BMI Category		
Underweight (<18.5)	4 (5.5%)	4 (5.5%)
Normal Weight (18.5–24.9)	15 (20.5%)	17 (33.3%)
Overweight (25.0–29.9)	16 (21.9%)	11 (21.6%)
Obesity (≥30.0)	38 (52.1%)	8 (15.7%)
Mean Duration of Disease (Weeks)	49.2 ± 7.10	37.2 ± 8.80
(Comorbidities) Hypertension		
Present	30 (41.1%)	17 (33.3%)
Absent	43 (58.9%)	34 (66.7%)
Smoking		
Present	28 (38.4%)	17 (33.3%)
Absent	45 (61.6%)	34 (66.7%)
Diabetes Mellitus		
Present	38 (52.4%)	27 (52.9%)
Absent	35 (47.6%)	24 (47.1%)
Biochemical Markers		
Elevated CRP	56 (76.7%)	11 (21.6%)
Elevated ESR	61 (83.6%)	11 (21.6%)
Raised Creatinine	12 (16.4%)	5 (9.8%)
Raised Bilirubin	30 (41.1%)	13 (25.5%)
Hypocalcemia	25 (34.2%)	6 (11.8%)
Hypomagnesemia	20 (27.4%)	5 (9.8%)

Among the 73 patients with hypoalbuminemia, 38 (52.1%) were classified as obese (≥30.0), with a p-value of 0.001. The mean duration of the disease (measured from the onset of symptoms) was found to be 49.2 ± 7.10 weeks, which also showed a significant correlation (p=0.01). Hypoalbuminemia in colorectal cancer patients was strongly associated with obesity (52.1%, p=0.001) and elevated inflammatory markers, including CRP (76.7%, p=0.001) and ESR (83.6%, p=0.001). A moderate association was observed with longer disease duration (49.2 weeks, p=0.01), hypocalcaemia (34.2%, p=0.01), and hypomagnesemia (27.4%, p=0.02), highlighting the roles of systemic inflammation, chronic illness, and nutritional imbalances in its development (Table 3).

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Table 3: Prevalence of Hypoalbuminemia and Clinical Correlations(n=73)

Characteristics	Hypoalbuminemia (n=73)	p-value
Obesity (≥30.0)	38 (52.1%)	0.001
Mean Duration of Disease (Weeks)	49.2 ± 7.10	0.01
Elevated CRP	56 (76.7%)	0.001
Elevated ESR	61 (83.6%)	0.001
Hypocalcemia	25 (34.2%)	0.01
Hypomagnesemia	61 (83.6%)	0.02

DISCUSSION

The prevalence of hypoalbuminemia in this study was 58.9%, a figure consistent with global reports on CRC patients. The study identified key associations of hypoalbuminemia with factors such as obesity, prolonged disease duration, elevated inflammatory markers (CRP and ESR), and biochemical disturbances, notably hypocalcaemia and hypomagnesemia. In terms of prevalence, the rate of hypoalbuminemia observed in this study (58.9%) closely matches that reported in similar populations globally. A study from South Korea found that 55% of CRC patients undergoing surgery had hypoalbuminemia, a figure nearly identical to this study [14]. The high prevalence can be attributed to a combination of chronic inflammation, cancer-related cachexia, and malnutrition common factors in CRC patients worldwide. The association between obesity (BMI ≥30.0) and hypoalbuminemia observed in the current study contributes to the expanding research on the obesity paradox in cancer patients. Despite being categorized as obese, patients in the cohort displayed hypoalbuminemia, a phenomenon that has been similarly reported in other studies. For instance, one review done by a Cancer Research Group in Spain found that obesity and malnutrition coexist in cancer patients due to metabolic dysregulation and systemic inflammation [15]. This contrasts with findings from a multicentre study conducted in China, where underweight patients are often at a higher risk of hypoalbuminemia [16]. In the current study, inflammation—indicated by elevated C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) was strongly linked to hypoalbuminemia. Specifically, 76.7% of patients with hypoalbuminemia had elevated CRP levels, and 83.6% showed elevated ESR levels. These results are consistent with international research that emphasizes the significant role of systemic inflammation in the onset of hypoalbuminemia in cancer patients. For example, a meta-analysis by Sofic et al., in 2021 confirmed that elevated CRP and ESR are key predictors of hypoalbuminemia in colorectal cancer (CRC) patients, suggesting that chronic inflammation caused by the tumour or cancer-related cachexia contributes to lower albumin levels [17]. The inflammatory response, often persistent in CRC patients, triggers the release of cytokines such as IL-6 and TNF-α, which inhibit albumin production and increase protein breakdown, worsening malnutrition and hypoalbuminemia [18]. A study in Saudi Arabia by Almasaudi et al., has also observed significant associations between hypoalbuminemia and low calcium and magnesium levels in cancer patients, suggesting a multifaceted origin of these imbalances involving poor nutrition, inflammation, and the direct metabolic impact of cancer [11]. Interestingly, no significant relationship was found between hypoalbuminemia and age or residential background, implying that demographic factors may play a lesser role in its development among CRC patients. Instead, clinical factors such as disease duration, comorbidities, and inflammation seem to have a greater influence on serum albumin levels [19]. These findings underscore the importance of a holistic approach to managing hypoalbuminemia in CRC patients, focusing not only on nutritional interventions but also on controlling systemic inflammation and addressing comorbidities [20]. Clinically, these associations underscore the need for early nutritional and inflammatory management strategies to improve patient outcomes and mitigate complications associated with hypoalbuminemia. However, the relatively small sample size and single-centre design may limit the generalizability of the results to broader populations.

CONCLUSIONS

It was concluded that hypoalbuminemia is frequently observed in colorectal cancer patients and is significantly associated with obesity, longer disease duration, rural residency, elevated inflammatory markers (CRP and ESR), and electrolyte imbalances (hypocalcemia and hypomagnesemia). These findings highlight the important roles of systemic inflammation and metabolic dysfunction in the development of hypoalbuminemia within this population. Clinically, these associations underscore the need for early nutritional and inflammatory management strategies to improve patient outcomes and mitigate complications associated with hypoalbuminemia.

Authors Contribution

Conceptualization: TN
Methodology: TN, SN, AMB, AIM
Formal analysis: MM, FM
Writing review and editing: SN, AMB

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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