Original Article

Correlation of Pretreatment Hemoglobin and Platelet Counts with Clinicopathological Features in Colorectal Cancer in Saudi Population

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ABSTRACT

Background/Aims: In Saudi Arabia, colorectal cancers (CRCs) are registered as the second most common cancers. However, no data has been reported about correlation of the severity of the anemia and pretreatment platelets level with clinicopathological features of CRCs. We aimed to evaluate the association between pretreatment hemoglobin and platelets level and the clinicopathological features of CRC patients in Saudi Arabia. **Materials and Methods:** Between September 2005 and November 2011, One hundred and fifty-four confirmed CRC patients underwent thorough physical examination, blood investigations, endoscopic ultrasonography (EUS), and computed tomography (CT) for staging before surgery. Findings of physical assessment, EUS, CT, and pathological specimens were correlated with pretreatment hemoglobin and platelets levels the Pearson–Kendall tau correlative coefficients. **Results:** The mean age of cohort was 56.6 years (range: 26-89). Left-sided CRC were predominant (97 patients; 63%). Mean size of primary tumor was 6 cms (1–18) SD ± 3.55. Mean values of hemoglobin, red blood cells, hematocrit, white blood cells, and platelets were 11.9 SD ± 2.3, 35.5 SD ± 5.7, $4.43 \times 10^6/mL$ SD ± 0.6, $7.67 \, 10^6/mL$ SD ± 2.44, and $343 \times 10^3/mL$ SD ± 164.4, respectively. Pretreatment hemoglobin was inversely correlated with primary tumor size (R: 0.71, R^2: 1.55, $P = 0.0001$) and nodal status (R: 0.02, R^2: 0.05, $P = 0.01$). Right-sided CRC had significantly low pretreatment hemoglobin levels ($P = 0.001$). Interestingly, pretreatment thrombocytosis was seen only in right-sided CRC ($P = 0.0001$). **Conclusion:** Pretreatment anemia and thrombocytosis were found mainly in right-sided CRCs and advanced primary and nodal stages. Pretreatment hemoglobin and thrombocytosis can be considered as useful prognostic markers in CRC patients.

Key Words: Colorectal cancers, correlation, pretreatment hemoglobin levels, platelet counts, Saudi population

Colorectal cancers (CRCs) are ranked as the third most common cancers in males and the second in females worldwide.[1] Anemia has been reported as a common clinical manifestation in CRC patients.[2] Iron-deficiency anemia (IDA) is the most present type of anemia in CRC patients, and it has been reported as an important prognostic predictor of CRC.[3-8] Data have shown a strong association between the CRC and the IDA. Many studies have been researched about the pretreatment hemoglobin level in CRC patients in different tumor stages.[9] In Saudi Arabia, CRC are registered as the second most common cancers in 2007.[10] However, there is limited data about association of pretreatment hemoglobin levels with different tumor size, primary staging and nodal staging in our population. A Norwegian study showed that among 1189 of the referred patients with CRC, 74.7% patients suffered from anemia. The study concluded that anemia is common and associated with T-stage of tumor neither N-stage nor M-stage.[11] Another study showed that 87.2% (75 out of 86) patients with right colon cancer had anemia. This study recommended right colon examination in any patient with IDC.[12]

Similarly, recent studies have shown that pretreatment thrombocytosis (platelet count > 400×10^9/L) is a poor prognostic factor in CRC patients.[13]

In the present study, we investigated the frequency of pretreatment hemoglobin level and platelet counts in CRC patients and association with location, size, and different tumor stages in Saudi population using hospital registry data.

MATERIALS AND METHODS

After the approval from Institutional Ethical Review Board (IRB) committee, the prospective study on 154 patients with CRCs who were treated during September 2005 to November 2011 with or without neoadjuvant chemotherapy/chemoradiation by surgery and adjuvant chemotherapy, comprised the study population. Inclusion criteria were (1) histopathologically confirmed CRC patients; (2) T1–T4, N0–N2; (3) pretreatment hematological tests and staging workup including endoscopic ultrasonography (EUS), computed tomography (CT) chest, abdomen, and pelvis, magnetic resonance imaging (MRI) abdomen, and pelvis; and (4) underwent surgical resection with or without neoadjuvant/adjuvant chemotherapy and radiotherapy. Exclusion criteria were (1) presence of distant metastasis and (2) incomplete details in medical charts.

Clinical variables

Clinical features including age, gender, baseline carcinoembryonic antigen (CEA) levels, location of CRC, initial tumor size on physical, EUS, CT, and MRI imaging and pretreatment hematology (red blood cells, white blood cells, hemoglobin, mean corpuscular volume, mean corpuscular hemoglobin concentration, hematocrit, platelets) were studied. Surgery was performed based on location of tumor (anterior resection, abdominoperineal resection, or hemicolectomy).

Preoperative assessment of tumor size

In all 154 CRC patients, preoperative assessment by physical examination, EUS, CT, and MRI was done. All physical examinations, EUS, CT, and MRI were performed by experienced oncologists and radiologists. All measurements of primary tumor size were taken on long axis of diameter and noted down on data collection proforma.

Postoperative assessment of tumor size

After surgical resection, CRC specimens were placed in 10% formalin overnight and were examined by experienced pathologist after the specimen were cut along their longest axis, stained with hematoxylin and eosin and measurements of primary tumor and lymph nodes were made and noted down on data collection proforma.

Statistical analysis

Mean, median, and mode of pretreatment hemoglobin, platelets, and different tumor sizes, and location is described. The correlation between pretreatment hemoglobin and platelets with different T and N stages were estimated by the Pearson/Kendall tau correlative coefficients. The mean differences and limits of agreement corresponding to the 95% confidence interval (95% CI) were analyzed. All statistical analyses were performed using the computer program SPSS version 16.0.

RESULTS

Clinical characteristics

Patients' clinical and treatment characteristics are shown in Table 1. Mean age of cohort was 56.60 years [range: 26-89; standard deviation (SD) ±13.7]. According to gender, cohort was predominantly male (76.6%). According to comorbidities, 72 patients (46.7%) had diabetes (26%), hypertension (9%), or combined with dyslipidemia (4%). Family history was positive in 21 patients (13.6%). Majority of cohort (108 patients; 70.1%) had left-sided CRC (rectum, sigmoid, rectosigmoid, and descending colon). Mean size of primary tumor was 6 cm (1-18) SD ± 3.55. Mean values of hemoglobin, red blood cells, hematocrit, white blood cells, and platelets were 11.9 SD ± 2.3, 35.5 SD ± 5.7, 4.43×10^6/mL SD ± 0.6, 7.67 10^6/mL SD ± 2.44, and 343×10^3/mL SD ± 164.4, respectively.

Correlation of pretreatment hemoglobin with tumor location, size, and staging

Pretreatment hemoglobin levels were found significantly lower in right-sided colonic carcinomas ($P = 0.001$) [Figure 1 and Table 2]. Pretreatment hemoglobin levels were found inversely correlated with T (R: -0.77, R^2: -1.55, $P = 0.0001$) and N stage (R: -0.02, R^2: -0.053, $P = 0.01$), respectively [Figure 2a and b].
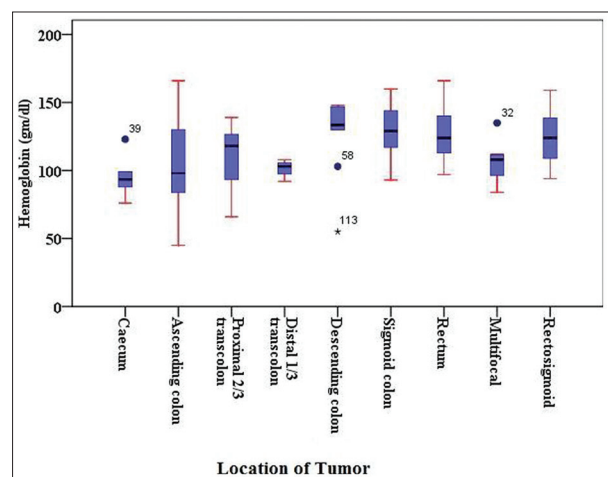

Figure 1: Pretreatment hemoglobin levels and tumor location

Table 1: Patient's characteristics

Variables	N (%)
Age (years)	56.60 (26-89) SD±13.7
Gender (%)	
Male	118 (76.6)
Female	36 (23.4)
Baseline CEA level (ng/mL) (%)	
<5	90 (58.5)
>5	64 (51.5)
Location (%)	
Rectum	42 (27.2)
Sigmoid	30 (19.5)
Recto-sigmoid	25 (16.2)
Descending colon	11 (7.1)
Distal 1/3rd transverse colon	3 (1.9)
Proximal 2/3rd transverse colon	8 (5.2)
Ascending colon	18 (11.8)
Cecum	8 (5.2)
Multifocal	9 (5.9)
Primary tumor size (cm)	6 (1-18) SD±3.55
LVSI (%)	
Yes	28 (19.4)
No	116 (80.6)
Grade (%)	
I	44 (28.6)
II	74 (48.0)
III	36 (23.4)
Clinical T stage (%)	
cT1	6 (3.9)
cT2	59 (38.3)
cT3	77 (50.0)
cT4	12 (7.8)
Clinical N stage (%)	
cN0	97 (63.0)
cN1	41 (26.6)
cN2	16 (10.4)
Clinical TNM staging (%)	
T1N0M0	6 (4.0)
T2N0M0	47 (30.5)
T2N1M0	12 (7.8)
T3N0M0	36 (23.4)
T3N1M0	27 (17.5)
T3N2M0	13 (8.4)
T3N3M0	1 (0.65)
T4N0M0	7 (4.5)
T4N1M0	3 (1.9)
T4N2M0	2 (1.3)
Neoadjuvant therapy (%)	
Chemotherapy	67 (43.5)
CCRT	87 (56.5)
Baseline hematology	
Hemoglobin (g/dL)	11.9 (4.5-16.6) SD±23.2
Hematocrit (%)	35.5 (16-48.9) SD±5.7
MCV	80.94 (49.1-92.9) SD±7.9
MCH	27.2 (13.9-33.0) SD±3.54
MCHC (%)	33.5 (28.2-36.1) SD±14.5

Contd....

Table 1: Contd...

Variables	N (%)
RBC (×10⁶/mL)	4.43 (3.1-6.1) SD±0.6
Platelets	343 (115-1356) SD±164.4
WBC	7.67 (3.4-19.4) SD±2.44

CEA: Carcinoembryonic antigen, LVSI: Lymphovascular space invasion, TNM: Tumor, node, metastasis, CCRT: Concurrent chemoradiation, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, RBC: Red blood cells, WBC: White blood cells

Table 2: Clinicopathological features according to pretreatment hemoglobin levels

Variables	Platelets<450 (n=123) (79.2%)	Platelets>450 (n=31) (20.8%)	P value
Mean age	55.4 years	56.4 years	0.9
Gender (%)			
Male	95 (77.3)	23 (74.2)	0.7
Female	28 (22.7)	8 (25.8)	0.8
Location (%)			
Rectum	37 (30.0)	5 (16.1)	0.05
Sigmoid	24 (19.5)	6 (19.4)	0.9
Recto-sigmoid	22 (17.9)	3 (9.7)	0.05
Descending colon	9 (7.3)	2 (6.4)	0.8
Distal 1/3rd transverse colon	1 (0.8)	2 (6.4)	0.03
Proximal 2/3rd transverse colon	7 (5.7)	1 (3.2)	0.06
Ascending colon	11 (8.9)	7 (22.6)	0.01
Caecum	6 (4.9)	2 (6.4)	0.7
Multifocal	5 (4.0)	4 (13.0)	0.05
T stage (%)			
cT1	5 (4.0)	1 (3.2)	0.8
cT2	46 (37.4)	13 (42.0)	0.9
cT3	66 (53.7)	11 (35.5)	0.06
cT4	6 (4.9)	6 (19.4)	0.03
N stage (%)			
cN0	76 (61.8)	21 (67.8)	0.9
cN1	33 (26.8)	8 (25.8)	0.8
cN2	14 (11.4)	2 (6.4)	0.6
TNM stage (%)			
T1N0M0	5 (4.0)	1 (3.2)	0.8
T2N0M0	37 (30.0)	10 (32.3)	0.8
T2N1M0	9 (7.3)	3 (9.7)	0.9
T3N0M0	31 (25.2)	5 (16.1)	0.06
T3N1M0	23 (18.7)	4 (26.0)	0.05
T3N2M0	11 (8.9)	2 (6.4)	0.7
T3N3M0	1 (0.8)	-	0.9
T4N0M0	2 (1.6)	5 (16.1)	0.02
T4N1M0	2 (1.6)	1 (3.2)	0.05
T4N2M0	2 (1.6)	-	0.8
LVSI (%)			
Positive	8 (20.5)	20 (64.5)	0.001
Negative	115 (79.5)	11 ((35.5)	0.001

LVSI: Lymphovascular space invasion, c: clinical, TNM: Tumor, node, metastasis, HB: Hemoglobin

Correlation of pretreatment platelet level with tumor location, size, and staging

Pretreatment platelet levels were found significantly high in right-sided colonic carcinomas Figure 3, however, no correlation was found between pretreatment platelet levels and T or N stage [Table 3].

DISCUSSION

In our study, pretreatment hemoglobin levels were found significantly lower in right-sided colon carcinoma as compared to left-sided tumors; these findings have also been reported by other studies.[11-13] Saidi *et al.* reported in 253 CRC patients that preoperative hemoglobin levels were significantly lower for right-sided lesions (*P* = 0.05),

however, there was no relationship of pretreatment hemoglobin level to the stage of disease at presentation contrary to our findings.[14]

Furthermore, in our study pretreatment platelet levels were found significantly high in right-sided colonic cancer. Platelet count has been reported to have predictive value in various cancers including CRC, and increased platelet levels have been postulated as one of the mechanisms of hematogenous spread of metastases.[15] One study reported that pretreatment platelet counts were correlated with right-sided colon cancers, venous invasion, and tumor size, and also it strongly correlated with the response rate. Furthermore, patients with pretreatment thrombocytosis had significantly shorter local recurrence-free survival.[16]
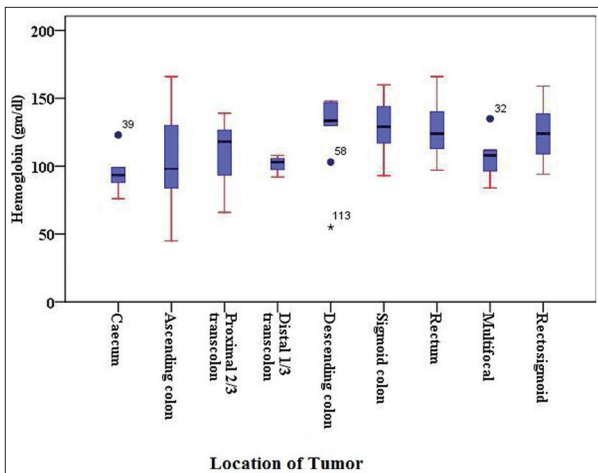

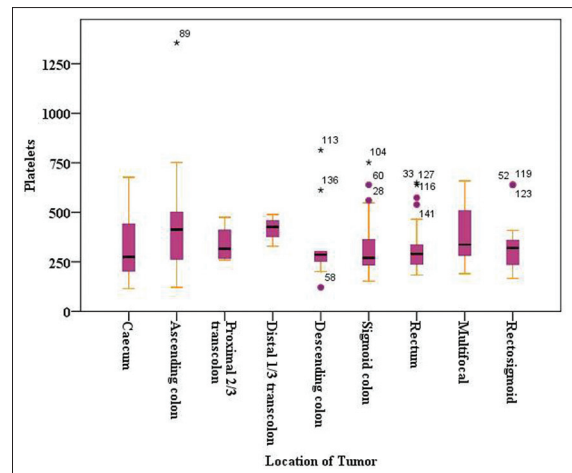**Figure 1:** Pretreatment hemoglobin levels and tumor location

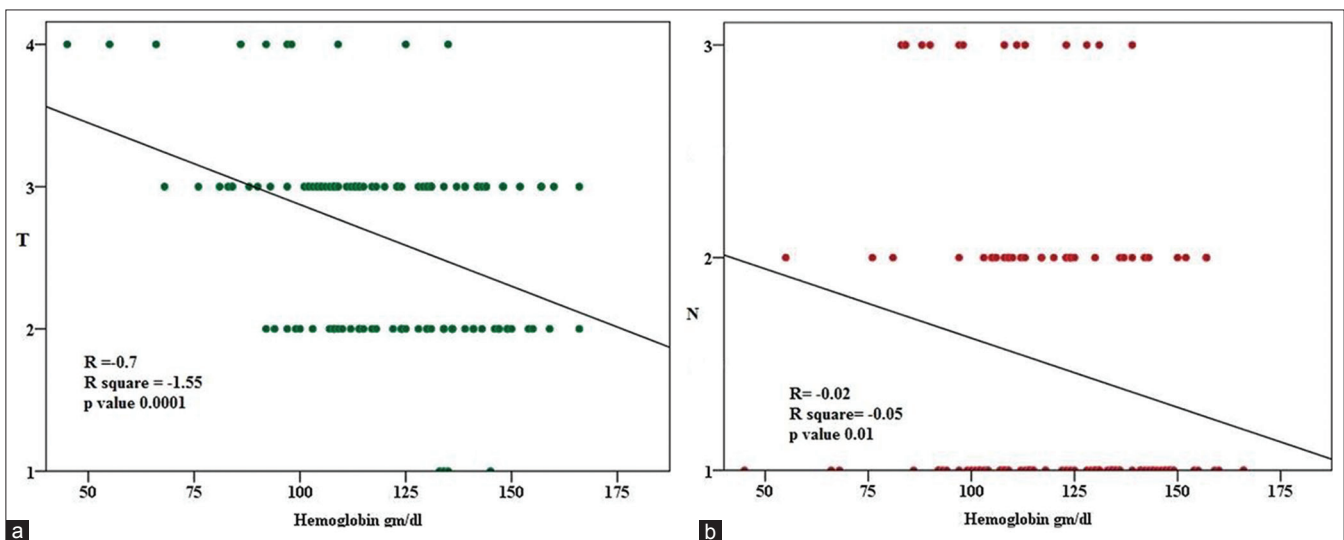**Figure 3:** Pretreatment platelet counts and tumor location

Figure 2: (a) Correlation of pretreatment hemoglobin with T stage and (b) N stage

Table 3: Clinicopathological features according to pretreatment platelet levels

Variables	Platelets<450 (*n*=123) (79.2%)	Platelets>450 (*n*=31) (20.8%)	*P* value
Mean age	55.4 years	56.4 years	0.9
Gender (%)			
Male	95 (77.3)	23 (74.2)	0.7
Female	28 (22.7)	8 (25.8)	0.8
Location (%)			
Rectum	37 (30.0)	5 (16.1)	0.05
Sigmoid	24 (19.5)	6 (19.4)	0.9
Recto-sigmoid	22 (17.9)	3 (9.7)	0.05
Descending colon	9 (7.3)	2 (6.4)	0.8
Distal 1/3rd transverse colon	1 (0.8)	2 (6.4)	0.03
Proximal 2/3rd transverse colon	7 (5.7)	1 (3.2)	0.06
Ascending colon	11 (8.9)	7 (22.6)	0.01
Caecum	6 (4.9)	2 (6.4)	0.7
Multifocal	5 (4.0)	4 (13.0)	0.05
T stage (%)			
cT1	5 (4.0)	1 (3.2)	0.8
cT2	46 (37.4)	13 (42.0)	0.9
cT3	66 (53.7)	11 (35.5)	0.06
cT4	6 (4.9)	6 (19.4)	0.03
N stage (%)			
cN0	76 (61.8)	21 (67.8)	0.9
cN1	33 (26.8)	8 (25.8)	0.8
cN2	14 (11.4)	2 (6.4)	0.6
TNM stage (%)			
T1N0M0	5 (4.0)	1 (3.2)	0.8
T2N0M0	37 (30.0)	10 (32.3)	0.8
T2N1M0	9 (7.3)	3 (9.7)	0.9
T3N0M0	31 (25.2)	5 (16.1)	0.06
T3N1M0	23 (18.7)	4 (26.0)	0.05
T3N2M0	11 (8.9)	2 (6.4)	0.7
T3N3M0	1 (0.8)	-	0.9
T4N0M0	2 (1.6)	5 (16.1)	0.02
T4N1M0	2 (1.6)	1 (3.2)	0.05
T4N2M0	2 (1.6)	-	0.8
LVSI (%)			
Positive	8 (20.5)	20 (64.5)	0.001
Negative	115 (79.5)	11 ((35.5)	0.001

LVSI: Lymphovascular space invasion, c: Clinical, TNM: Tumor, node, metastasis

The limitation of our study was that we did not assess the correlation between pretreatment hemoglobin and platelets and locoregional control and distant control because our primary objective was to evaluate the association between pretreatment hemoglobin and platelet counts and the clinicopathological features of CRC patients in Saudi population.

In conclusion, pretreatment anemia and thrombocytosis were found mainly in right-sided CRC and advanced primary and nodal stages. Pretreatment hemoglobin and thrombocytosis can be considered as useful prognostic markers in CRC patients in future studies.

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