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

Eyad F. Al-Saeed, Mutahir A. Tunio1, Omar Al-Obaid2, Maha Abdulla3, Alaa Al-Anazi4, Jumanah Al-Shanifi4, Leena Al-Ameer4, Tarfah Al-Obaidan4

Consultant Radiation Oncology, 2Consultant Colorectal Surgery, 3Colorectal Center, King Khalid University Hospital, King Saud University, 1Radiation Oncology, Comprehensive Cancer Center, King Fahad Medical City, 4Medical Students, King Saud University, Riyadh, Saudi Arabia

Address for correspondence:
Dr. Mutahir Ali Tunio, Radiation Oncology, Comprehensive Cancer Center, King Fahad Medical City, Riyadh - 59046, Saudi Arabia. E-mail: mkhairuddin@kfmc.med.sa

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 × 106/mL SD ± 0.6, 7.67 106/mL SD ± 2.44, and 343 × 103/mL SD ± 164.4, respectively. Pretreatment hemoglobin was inversely correlated with primary tumor size (R: 0.71, R²: 1.55, P = 0.0001) and nodal status (R: 0.02, R²: 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

Received: 08.09.2013, Accepted: 03.11.2013
How to cite this article: Al‑Saeed EF, Tunio MA, Al‑Obaid O, Abdulla M, Al‑Anazi A, Al‑Shanifi J, et al. Correlation of pretreatment hemoglobin and platelet counts with clinicopathological features in colorectal cancer in Saudi population. Saudi J Gastroenterol 2014;20:134‑8.

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 57.2% (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 (\(P = 0.001\)) \([\text{Figure 1 and Table 2}]\). 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 \([\text{Figure 2a and b}]\).
### 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 |

### Table 1: Contd...

| Variables                      | N (%)   |
|--------------------------------|---------|
| RBC (×10^6/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) | Platelets>450 (n=31) | 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

Contd....
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. 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.

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. 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.
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.

**REFERENCES**

1. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global Cancer Statistics. CA: Cancer J Clin 2011;61:69-90.
2. Edna TH, Karlsen V, Jullumstro E, Lydersen S. Prevalence of anaemia at diagnosis of colorectal cancer: Assessment of associated risk factors. Hepatogastroenterology 2012;59:713-6.
3. Goodman D, Irvin TT. Delay in the diagnosis and prognosis of carcinoma of the right colon. Br J Surg 1993;80:1327-9.
4. Hamilton W, Lancashire R, Sharp D, Peters TJ, Cheng KK, Marshall T. The importance of anaemia in diagnosing colorectal cancer: A case–control study using electronic primary care records. Br J Cancer 2008;98:323-7.
5. Curless R, French JM, Williams GV, James OF. Colorectal carcinoma: Do elderly patients present differently? Age Ageing 1994;23:102-7.
6. Majumdar SR, Fletcher RH, Evans AT. How does colorectal cancer present? Symptoms, duration, and clues to location. Am J Gastroenterol 1999;94:3039‑45.
7. Roncoroni L, Pietra N, Violi V, Sarli L, Choua O, Peracchia A. Delay in the diagnosis and outcome of colorectal cancer: A prospective study. Eur J Surg Oncol 1999;25:173‑8.
8. Young CJ, Sweeney JL, Hunter A. Implications of delayed diagnosis in colorectal cancer. Aust N Z J Surg 2000;70:635‑8.
9. Zhen L, Zhe S, Zhenning W, Zhifeng M, Zhidong L, Xiaoxia L, et al. Iron-deficiency anemia: A predictor of diminished disease-free survival of T3N0M0 stage colon cancer. J Surg Oncol 2012;105:371‑5.
10. Al‑Eid H, Manalo M. Cancer Incidence and Survival Report Saudi Arabia 2007. Saudi Cancer Registry, 2007. Available at http://www.scr.org.sa/. Accessed on August/3/2013.
11. Edna TH, Karlsen V, Jullumstro E, Lydersen S. Prevalence of anaemia at diagnosis of colorectal cancer: Assessment of associated risk factors. Hepatogastroenterology 2012;59:713-6.
12. Kanellos D, Kitsios G, Kanellos I, Demetriades H, Pramateftakis MG, Angelopoulos S, et al. Anaemia as a symptom of right colon cancer. Tech Coloproctol 2004;8 Suppl 1:s62‑4.
13. Kandemir EG, Mayadagli A, Karagoz B, Bilgi O, Turken O, Yaylaci M. Prognostic significance of thrombocytosis in node‑negative colon cancer. J Int Med Res 2005;33:228‑35.
14. Saidi HS, Karuri D, Nyaim EO. Correlation of clinical data, anatomical site and disease stage in colorectal cancer. East Afr Med J 2008;85:259-62.
15. Castillo‑Pérez JJ. Regarding the article "thrombocytosis as a predictor of distant recurrence in patients with rectal cancer. Arch Med Res 2013;44:77-8.
16. Kawai K, Kitayama J, Tsuho NH, Sunami E, Watanabe T. Thrombocytosis before pre-operative chemoradiotherapy predicts poor response and shorter local recurrence‑free survival in rectal cancer. Int J Colorectal Dis 2013;28:527-35.

**Table 3: Clinicopathological features according to pretreatment platelet levels**

| Variables                       | Platelets<450 (n=123) | Platelets>450 (n=31) | 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)             |         |
| 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     |
| LVSII (%)                       |                       |                      |         |
| Positive                        | 8 (20.5)              | 20 (64.5)            | 0.001   |
| Negative                        | 115 (79.5)            | 11 (35.5)            | 0.001   |

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

Source of Support: Nil, Conflict of Interest: None declared.