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Original Research Article

# Predicting the Prognosis of Colorectal Cancer by Analysis of Haematological Parameters in Association with Histopathological Grading - In a Tertiary Care Centre

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## Abstract

***Introduction:*** Colorectal cancers are a major cause of cancer-related deaths around the world. The most common malignancy of the stomach, comprising more than 90% of all gastric cancers. Usually for staging colon cancers preoperatively, radiological images and multiple blood tests are used**.** Radiological tests, on the other hand, are both difficult and costly to use. Efficient markers are needed for early diagnostic staging in colon cancers. In our study we aim at predicting the grade of colon cancer and prognosis preoperatively by analysing the hematological parameters, which are simple, cost effective and easy to apply. ***Materials and method:*** A retrospective study was carried out in line with research regulations, including the approval of the Ethical committee. This study included 61 patients operated in tertiary care hospital during the period of January 2018 and January 2021.For the diagnosis of colorectal cancer, the clinical data was obtained from histopathology request forms, department of radiology and histopathological examination. The hematological parameters were generated from Sysmex XN 1000 autoanalyser. These hematological parameters (hemoglobin, RBC count, MPV, PLR, NLR, PCV, MCV, MCHC, RDW, Platelets, TLC, Absolute neutrophil count, neutrophils, lymphocytes, monocytes, eosinophils, basophils ) were standardized by routine external and internal quality control checks. ***Results:*** In this study, gender and age distribution, female patients were predominant and age group between 51 to 60 was commonly affected. Colorectal cancer was graded based on histopathological differentiation, 19 were found to be of grade1, 27 patients of grade 2 and 15 patients of grade 3. Majority of colorectal cancer were histological grade 2. On correlation, there was significant increase in total leucocyte count, platelet count, MPV, PLR, NLR in higher grades of colorectal cancer. Moreover, there was decrease in haemoglobin, PCV, RDW in higher grades of colorectal cancer. ***Conclusion***: Since hematological parameters are easily accessible inflammatory markers, they may be used to determine the prognosis of the colorectal cancer in association with histopathological grading of cancer.

**Keywords:** Colorectal cancer, haematological parameters, grades, hemicolectomy.



## INTRODUCTION

Colorectal cancers are a major cause of cancer-related deaths around the world. The annual incidence rates (AARs) of colon cancer and rectal cancer. Most common site of colon cancer is right side colon cancer than left side. Risk factors are older age group, African-American race, chronic smokers and alcoholics, family history of colorectal cancer or polyps, intestinal inflammatory conditions (Inflammatory bowel disease and Crohn's disease), inherited syndromes that increase colon cancer risk. Usually for staging colon cancers preoperatively, radiological images and multiple blood tests are used**.** Radiological tests, on the other hand, are both difficult and costly to use. Efficient markers are needed for early diagnostic grading in colon cancers. In our study we aimed at predicting the prognosis of colon cancer by preoperatively assessing the hematological parameters, which are simple, cost effective and easy to apply.

## PATIENTS AND METHODS

A retrospective study was carried out in line with research regulations, including the approval of the Ethical committee this study included 61 patients operated in tertiary care hospital during the period of January 2018 and January 2021.The diagnosis of

colorectal cancer was based on clinical history, radiological diagnosis and histopathology reports. The hematological parameters were generated from Sysmex XN 1000 autoanalyser. These hematological parameters (hemoglobin, RBC count, MPV, PLR, NLR, PCV, MCV, MCHC, RDW, Platelets, TLC, Absolute neutrophil count neutrophils, lymphocytes , monocytes, eosinophils, basophils) were standardized by routine external and internal quality control checks.

The preoperative haematological parameters were obtained for these patients and correlated with the colorectal cancer grades (based on differentiation) that were obtained from the postoperative histopathological reports.

**Inclusion Criteria**

This study included both colon cancer and rectal cancer patients. Other than surgical specimens, colon and rectal biopsies were also included.

**Exclusion Criteria**

This study excluded patients with benign and inflammatory conditions. The TNM staging is not considered.

**Statistical analysis**

The SPSS, version 19 software was used for the processing data. All the values were expressed as mean±standard deviation unless otherwise indicated. The differences in the mean values between the groups were analyzed by using the Student's t-test. A p-value of <0.05was considered statistically significant.The study was approved by the Saveetha institutional ethical committee

## RESULTS

In our study, out of 61 patients, male patients were 28(46%) and female patients were 33(54%), female population was predominant (Fig.1). On age distribution ,1 patient(1.8%) between the age group of 21-30 years, 5 patients(8.2%) between 31-40 years,11 patients (18%)between 41-50 years, 22patients(36%) between the age group of 51-60 years, and 16 patients(26%) were 61-70 years 6 patients (10%) betweeen71-80 years. Patients of the age group 51 to 60 years were predominantly affected (Fig.1).

Grades of colorectal cancer patients were categorized by clinical history, hematological parameters, radiological diagnosis and histopathological reports. Colorectal cancerwere graded based on histopathological differentiation as well differentiated, moderately differentiated and poorly differentiated (Fig.2 and3). In our study19 were found to be of grade1 (31%), 27 patients of grade2 (44%) and 15 patients of grade3 (25%).Majority of colorectal cancer were histological grade 2.

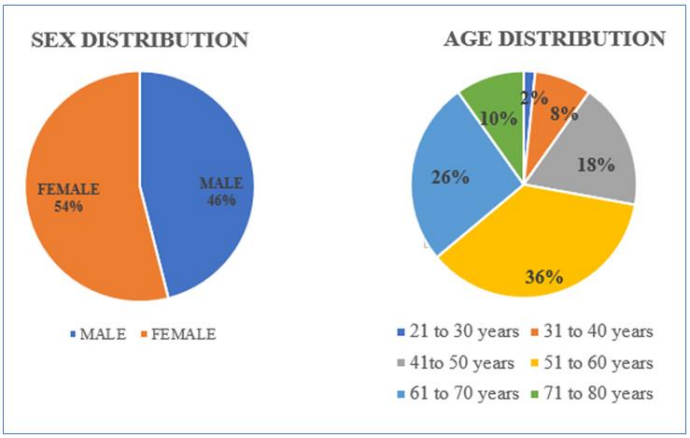


**Fig-1: Sex and Age distribution among colorectal cancer patients**

**Table-1: Age, sex and grade distribution**

| **Age** | **51 to 60** |
|---|---|
| Gender | Female 54% Male 46% |
| Grade | I-19II-27 III-15 |
| Surgery /procedure | Right hemicolectomy-15; Left hemicolectomy- 5;<br>Transverse resection-1;Sigmoidectomy-2;<br>Abdominoperineal resection-6; Colon biopsies-14; Rectal biopsies-18 |

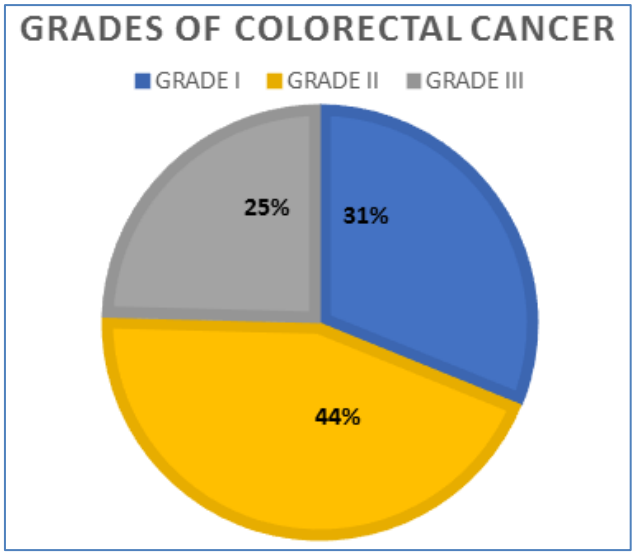


**Fig-2**

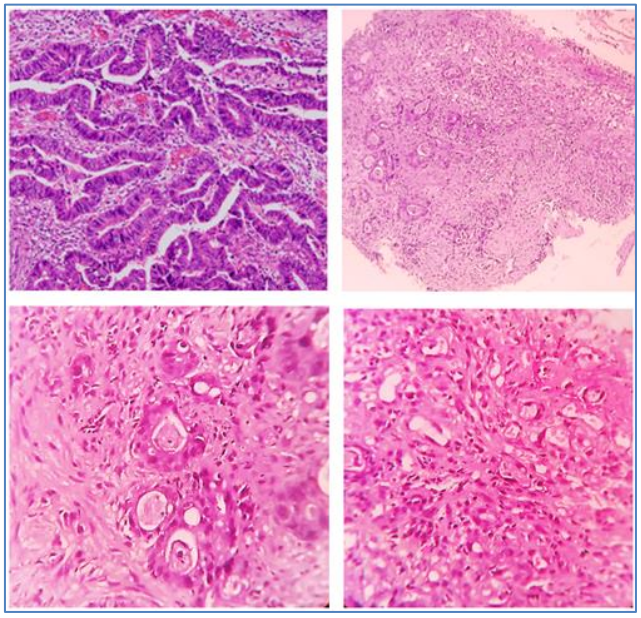

**Fig-3: Colorectal cancer of various grades based on differentiation**

(a)Well differentiated (grade1) (b) Lower magnification, moderately differentiated (grade2) (c) Moderately differentiated (d) poorly differentiated-signet ring cells (grade3)

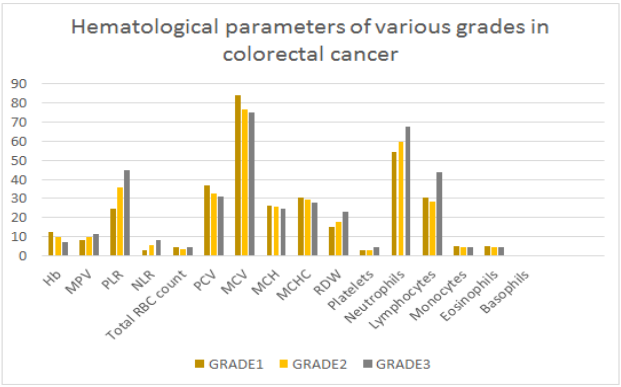


**Fig-4**

**Table-2: Correlation of hematological parameters in different gardes of colorectal cancer**

| | Grade1 | Grade2 | Grade3 |
|---|---|---|---|
| **Hb** | 12.184±1.597 | 9.893±1.131 | 7.340±1.467 |
| **MPV** | 8.437±1.513 | 9.596±1.595 | 11.520±1.125 |
| **PLR** | 24.545±5.561 | 35.697±2.072 | 44.981±5.639 |
| **NLR** | 3.150±1.524 | 5.615±2.893 | 8.236±1.484 |
| **Total RBC count** | 4.439±0.779 | 3.231±0.778 | 3.201±0.903 |
| **PCV** | 36.837±5.741 | 32.430±5.057 | 31.080±3.815 |
| **MCV** | 84.132±6.289 | 76.411±6.660 | 75.240±9.016 |
| **MCH** | 25.974±2.088 | 25.441±1.925 | 24.607±2.564 |
| **MCHC** | 30.432±1.568 | 29.359±1.934 | 27.727±1.951 |
| **RDW** | 14.921±2.270 | 17.756±6.099 | 22.913±8.159 |
| **Platelets** | 2.867±0.907 | 3.276±0.730 | 4.715±2.236 |
| **TLC** | 7191.053±2296.727 | 7534.815±944.255 | 8914±1090.398 |
| **Neutrophils** | 54.467±3.673 | 59.774±9.306 | 67.647±10.093 |
| **Lymphocytes** | 30.505±5.324 | 32.878±3.803 | 43.707±14.451 |
| **Monocytes** | 5.226±0.623 | 4.393±1.424 | 4.375±1.940 |
| **Eosinophils** | 4.811±2.687 | 4.458±1.915 | 4.733±1.940 |
| **Basophils** | 0.189±0.057 | 0.193±0.114 | 0.273±0.171 |
| **Absolute Neutrophil count** | 4710.526±1235.275 | 5649.259±1864.62 | 7822.667±2527.391 |

On correlation of mean haemoglobin with grades of colorectal patients, value among grade1 was12.184±1.597, grade2 was 9.893±1.131and grade3 was 7.340±1.467. As the grades increases, there is a decrease in hemoglobin values (Table.2 and Fig 4).

On correlation of mean PCV with grades of colorectal patients, value among grade1 was 36.837±5.741, grade2 was 32.430±5.057 and grade3 was 31.080±3.815.As the grades increases, there is decrease in PCV (Table.2).

On correlation of mean RDW with grades of colorectal patients, value among grade1 was 14.921±2.270, grade2 was 17.756±6.099 and grade3 was 22.913±8.159.As the grades increases, there is increase in RDW (Table.2).

On correlation of mean total leucocyte count (TLC) with grades of colorectal patients, value among grade1 was7191.053±2296.727, grade 2 was 7534.815±944.255 and grade3 was 8914±1090.398. As the grades increases, there is increase in TLC (Table.2).

On correlation of mean platelets with grades of colorectal patients, value among grade1 was 2.867±0.907, grade2 was 3.276±0.730 and grade3 was 4.715±2.236.As the grades increases, there is increase in platelet counts (Table.2).

On correlation of mean MPV with grades of colorectal patients, value among grade1 was 8.437±1.513, grade2 is 9.596±1.595 and grade3 11.520±1.125.As the grades increases, there is an increase in MPV (Table.2).

On correlation of mean PLR with grades of colorectal patients, value among grade1 was 24.545±5.561; grade 2 was35.697±2.072 and that of grade3 was 44.981±5.639.As the grades increases, there is increase in PLR (Table.2).

On correlation of mean NLR with grades of colorectal patients, value among grade1 was 3.150±1.524, grade2 was 5.615±2.893 and grade3 was 8.236±1.484.As the grades increases, there is increase in NLR (Table.2).

**Table-4: Correlation of hematological parameters of grade2 and grade3 colorectal cancer**

| PARAMETERS | GRADE 2 (mean±SD) | GRADE 3 (mean±SD) | P-VALUE |
|---|---|---|---|
| Hb | 9.893±1.131 | 7.340±1.467 | <0.001 |
| MPV | 9.596±1.595 | 11.520±1.125 | <0.001 |
| PLR | 35.697±2.072 | 44.981±5.639 | <0.001 |
| NLR | 5.615±2.893 | 8.236±1.484 | <0.001 |
| Total RBC count | 3.231±0.778 | 3.201±0.903 | 0.915 |
| PCV | 32.430±5.057 | 31.080±3.815 | 0.336 |
| MCV | 76.411±6.660 | 75.240±9.016 | 0.664 |
| MCH | 25.441±1.925 | 24.607±2.564 | 0.283 |
| MCHC | 29.359±1.934 | 27.727±1.951 | 0.014 |
| RDW | 17.756±6.099 | 22.913±8.159 | 0.043 |
| Platelets | 3.276±0.730 | 4.715±2.236 | 0.028 |
| TLC | 7534.815±944.255 | 8914±1090.398 | <0.001 |

A significant correlation was discovered between the mean values of hemoglobin, MPV, PLR, NLR, RBC count, PCV, MCV, MCHC, RDW and grading. The mean MCH was 25.974±2.088 in grade 1, and 25.441±1.925 in grade 2 (p=0.389) (Table 3).The mean platelet count was 2.867±0.907 in grade1 and 3.276±0.730 in grade 2. (Table 3)The mean TLC was 7191.053±2296.727 in grade1 and 7534.815±944.255 in grade 2. (Table 3). No significant correlation was observed between grading and MCH, TLC, platelet count.

**Table-4: Correlation of Hematological Parameters of Grade2 and Grade3 Colorectal Cancer**

| PARAMETERS | GRADE 1 (mean±SD) | GRADE 2 (mean±SD) | P-VALUE |
|---|---|---|---|
| Hb | 12.184±1.597 | 9.893±1.131 | <0.001 |
| MPV | 8.216±1.687 | 9.596±1.595 | 0.008 |
| PLR | 24.545±5.561 | 35.697±2.072 | <0.001 |
| NLR | 3.15±1.524 | 5.615±2.893 | <0.001 |
| Total RBC count | 4.439±0.779 | 3.231±0.778 | <0.001 |
| PCV | 36.837±5.741 | 32.430±5.057 | 0.011 |
| MCV | 84.132±6.289 | 76.411±6.660 | <0.001 |
| MCH | 25.974±2.088 | 25.441±1.925 | 0.384 |
| MCHC | 30.432±1.568 | 29.359±1.934 | 0.044 |
| RDW | 14.921±2.270 | 17.756±6.099 | 0.034 |
| Platelets | 2.867±0.907 | 3.276±0.730 | 0.113 |
| TLC | 7191.053±2296.727 | 7534.815±944.255 | 0.544 |

*Significant P≤0.05
**Highly Significant P≤0.01

A significant correlation was discovered between the mean values of hemoglobin, MPV, PLR, NLR, MCHC, RDW, platelet count and grading. The mean RBC count 3.231±0.778 in grade2 and 3.201±0.903 in grade3. (Table 4)The mean PCV was 32.430±5.057 in grade 2 and 31.080±3.815 in grade 3. (Table 4). The mean MCV was76.411±6.660 in grade1 and 75.240±9.016 in grade 2. (p=0.664) (Table 4) The mean MCH was 25.441±1.925 in grade 2, and 24.607±2.564 in grade 3 (p=0.283) (Table 4). No significant correlation was observed between grading and RBC count, PCV, MCV, MCH.

## DISCUSSION

Inflammation plays a crucial role in the tumorigenesis and growth processes. Local and systemic inflammatory reactions create an immune microenvironment which favors growth of cancer cells. Previously, systemic inflammation was reported in many studies as one of the important part of the carcinogenesis process. Systemic inflammation leads to release of several pro-inflammatory mediators, such as interleukin (IL)-1, IL-3 and IL-6, which stimulate megakaryocyte proliferation. Many studies have showed that the higher mortality is associated with elevated platelet count in several cancers. Thus, innate antitumor responses through cell- induced platelet aggregation which shields tumor cells from the major histocompatibility complex so as to escape immune surveillance by T cells. Hematological parameters reflect the balance between systemic inflammatory response and immune system function, which was also confirmed by several retrospective studies.

This study showed a proportional increase of platelet count, mean platelet volume (MPV) and platelet lymphocyte ratio (PLR) corresponding to higher grades of colorectal cancers. Platelet can stimulate the growth of tumor cells by aggregating and degranulating in tumor microvessels. Tumor-related inflammatory mediators can also stimulate platelet elevation.

We observed neutrophil lymphocyte ratio (NLR) is increased in higher histopathological grades of colorectal cancers. NLR has a balance between pro-tumor inflammation and anti-tumor immune function and its prognostic significance has been extensively studied but the significant reason for NLR raise with tumor progression has not been obtained.

We also observed that hemoglobin levels were reduced in higher grades of colorectal cancer. Low hemoglobin levels contribute to tumor hypoxia which is responsible for enhanced tumor growth. *Jing cui et al.*, reported that low hemoglobin levels as predictor of prognosis and survival in different cancerous diseases [8].

Platelet lymphocyte ratio is increased in higher grades. *Szkandera et al.* reported that the PLR was detected higher in patients with increased stage 3 colon cancer compared to stage 2 patients, and the cancer recurrence was observed earlier in patients with high PLR status [9]. *Erkan Karacan et al.*, a proportional increase was observed between the increase in platelet lymphocyte ratio and stagingof colon cancer [1].

Neutrophil lymphocyte ratio is *increased* in higher grades in this study. *Roxburgh et al.* study

revealed that high NLR are not only an indicator in cancer types, but also an independent factors in short survival [10]. *Szkandera et al.* reported that the increased NLR was shown to be correlated with an advanced TNM stage, early recurrence and bad survival [9].

## CONCLUSION

In this study, the female patients were affected commonly than male and there is variation in hematological parameters in association with grading of tumors. On correlation, there was significant increase in total leucocyte count, platelet count, MPV, PLR, NLR in higher grades of colorectal cancer. Moreover, there was decrease in haemoglobin, PCV, RDW in higher grades of colorectal cancer.As a result, these easily accessible inflammatory markers they may be used to determine the prognosis of the colorectal cancer in association with histopathological grading of cancer. However further studies with larger sample size are required to confirm the findings of the present study.

### Limitations in the study

There were some limitations in our study. Firstly, this was a retrospective study; therefore, complete information was not available for all the patients. Secondly, though our study was based on the data of the single tertiary care centre in Tamil Nadu, a large-scale study involving other Tertiary hospitals are required. Since, the number of patients in the study was low; we could not classify the patients according to the localization area of colorectal cancers.

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### Statement of Ethics

This study was approved by Ethics Committee of Saveetha Medical and Hospital (SMC/IEC/2021/07/259). As this study was a retrospective study, there was no patient's privacy data such as patient name, ID number, telephone and address were involved. Only demographic information and laboratory testing data of patients were collected and analyzed in this study.

### Disclosure Statement

All authors declared no conflicts of interest.

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