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Association of Carcinoembryonic Antigen, Hemoglobin, and Neutrophil to Lymphocyte Ratio with Colorectal Cancer Histopathological Grade in West Sumatra, Indonesia

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ABSTRACT

Colorectal cancer is a global health issue with a significant incidence and mortality rate. Identifying clinical characteristics using tumor biomarkers and hematological parameters is a crucial aspect in evaluating tumor cell differentiation grade. This study aims to determine the characteristics of Carcinoembryonic Antigen (CEA) levels, hemoglobin, and Neutrophil to Lymphocyte Ratio (NLR) values as indicators of histopathological differentiation grade in colorectal cancer patients. This was an observational, analytic study with a retrospective design, using medical record data from patients at Dr. M. Djamil General Hospital in Padang, from January 2023 to December 2024. A total of 154 patients meeting the inclusion and exclusion criteria were selected using a total sampling technique. Data were analyzed using statistical tests to assess the significance of the relationship between variables. The patient distribution showed a higher prevalence of females (55.8%), and more than half (62.3%) were aged 50 years or older. The histopathological profile was predominantly low grade (81.2%). Statistical test results showed a significant association between CEA levels and histopathological differentiation grade (p=0.017). However, no statistically significant association was found between hemoglobin levels (p=0.822) or NLR values (p=0.303) and histopathological differentiation grade. There is a potential association between CEA levels and histopathological differentiation grade, whereas hemoglobin levels and NLR values did not show a significant association. CEA levels can serve as a potential indicator in predicting tumor differentiation grade in colorectal cancer patients.

INTRODUCTION

Colorectal cancer (CRC) is a series of neoplastic transformations originating from the mucosal epithelium of the large intestine or colon to the rectum, occupying the third highest incidence and the second leading cause of death due to cancer globally (Sung et al., 2021). Cancer statistics in 2022 stated that the CRC phenomenon reached 1.93 million new cases and 935,000 deaths annually. (Siegel et al., 2022). A study conducted in Semarang indicated that screening and early detection efforts were challenging to implement, leading to diagnostic delays due to a lack of public awareness and limited access and facilities in peripheral areas, resulting in patients presenting to referral hospitals at advanced stages and worsening the poor prognosis (Purnomo et al., 2024).

Carcinoembryonic Antigen (CEA) is a glycoprotein on the oncofetal cell surface that functions as an adhesion molecule, which is usually expressed at low levels in normal adult colon tissue. (Kankanala et al., 2024). CEA expression will increase significantly in colorectal carcinoma cells in the intestinal lumen and will be released into the blood circulation (Shabo et al., 2025). Histopathological differentiation grade is another benchmark for assessing CRC cell malignancy, divided into low-grade and high-grade based on glandular differentiation. (Hasan et al., 2022). Observation conducted at Dr. M. Djamil Hospital, Padang, found a significant difference in CEA levels based on CRC histopathological differentiation grade (Asprilia et al., 2024). Cells with poor

differentiation grade tend to be aggressive and metastatic, and this correlates with high CEA levels (Mohammad et al., 2024).

Clinical manifestations frequently found in CRC patients are anemia, which occurs due to chronic occult bleeding, which generally occurs in right-sided colon tumors. Chronic blood loss, as well as chronic inflammatory mechanisms that inhibit erythropoiesis, cause a decrease in hemoglobin levels and worsen the patient's functional ability to the point of lowering tolerance towards oncology therapy (Joseph et al., 2022). The neutrophil-to-lymphocyte ratio (NLR) is a systemic inflammatory biomarker that influences cancer cell development, angiogenesis, and tumor cell metastasis, and can estimate patient prognosis. An increase in neutrophil count reflects the inflammatory response during tumor formation, while a decrease in lymphocyte levels indicates the presence of anti-tumor immunosuppression (Hamid et al., 2021).

Previous research by Asprilia et al. at Dr. M. Djamil Hospital, Padang, in 2024 found a significant difference in CEA levels by differentiation grade, with the low-grade group having a higher mean (67.72ng/mL) than the high-grade group. (Asprilia et al., 2024). This study had limitations because it used only a single biomarker, without integrating systemic response parameters such as NLR. Studies by Simatupang et al. and Iskandar et al. more often linked hematological profiles to clinical stages than to histopathological differentiation grades that describe tumor cell malignancy (Iskandar et al., 2023; Simatupang et al., 2025). Research by Aden et al. in Padang was limited to outlining general characteristics, rather than assessing complex variable correlations (Aden et al., 2025). The absence of research combining CEA, hemoglobin, and NLR as differentiation indicators creates a significant knowledge gap, as the combination of tumor markers and systemic inflammation can provide more precise predictions.

METHOD

This study used a retrospective, analytical, observational design to evaluate the relationship between variables. Researchers selected samples using a total sampling technique, according to inclusion and exclusion criteria. Inclusion criteria included patients diagnosed histopathologically with CRC who had complete data on CEA, hemoglobin, and leukocytes before therapy. Researchers excluded patients with a history of other malignancies, active infections, or hematological abnormalities, triggering data bias. The Ethics Committee of Dr. M. Djamil Hospital, Padang, approved this research protocol with a guarantee of data confidentiality (Ref: DP.04.03/D.XVI.10.1/356/2025).

Independent variables included CEA levels, hemoglobin, and Neutrophil to Lymphocyte Ratio (NLR). Non-smoker patients had normal CEA values <2.3ng/mL and high CEA values ≥2.3ng/mL. Smoker patients had normal values <4.1 ng/mL and high values ≥4.1ng/mL. (Joseph et al., 2022). Researchers established anemia limits <13 g/dL in males and <12g/dL in females (Gvirtzman et al., 2021). NLR values were classified as usual if <3.0 and increased if ≥3.0 based on the leukocyte differential count (Hamid et al., 2021). The dependent variable was histopathological differentiation grade, with low-grade and high-grade types (Hasan MF et al., 2022).

Researchers performed data analysis using SPSS software version 26.0. Descriptive analysis presented categorical data as frequencies and numerical data as Mean ± SD or median (minimum-maximum). Researchers tested data normality using the Kolmogorov-Smirnov test. Bivariate analysis evaluated the relationship of independent variables and histopathological grades using the Chi-Square test. A probability value (p-value) <0.05 indicated a statistically significant difference.

RESULTS

Table 1 demonstrates the dominance of the female gender, comprising 86 individuals (55.8%) of the total 154 samples. The 50-year-old age group accounted for the most significant proportion of cases, totaling 96 individuals (62.3%). Colorectal cancer patients had a normal body mass index (44.8%) and non-smoking status (60.4%).

Table 1. Frequency distribution of colorectal cancer patient characteristics based on gender, age, body mass index, and smoking status

Characteristics	f	%
Gender		
Male	68	44.2
Female	86	55.8
Age		
≥50 years	96	62.3
<50 years	58	37.7
BMI		
Underweight	24	15.6
Normal	69	44.8
Overweight	37	24.0
Obesity	24	15.6
Smoking status		
Non-smokers	93	60.4
Smokers	61	39.6

Table 2 shows high CEA levels in the low-grade group (76 individuals, 49.4%) and in the high-grade group (25 individuals, 16.2%). The normal CEA group comprised 49 low-grade individuals (31.8%) and 4 high-grade individuals (2.6%). The chi-square statistical test yielded a p-value = 0.017 ($p<0.05$). These results demonstrate a significant association between CEA levels and histopathological differentiation grades at Dr. M. Djamil Hospital, Padang, during the 2023-2024 period.

Table 2. Association between carcinoembryonic antigen levels and histopathological differentiation grades

CEA Levels	Histopathological differentiation		Total	p-value
	Low grade	High grade		
Normal	49 31.8%	4 2.6%	53 34.4%	0.017
Elevated	76 49.4%	25 16.2%	101 65.6%	
Total	125 81.2%	29 18.8%	154 100%	

Table 3 records anemia cases in the low-grade group (94 individuals, 61.1%) and in the high-grade group (23 individuals, 14.9%). The non-anemia group includes low-grade patients (31 individuals, 20.1%) and high-grade patients (6 individuals, 3.9%). The chi-square test yielded a p-value = 0.822 ($p>0.05$). These data indicate no significant relationship between hemoglobin levels and CRC histopathological differentiation grade.

Table 3. Association between hemoglobin levels and histopathological differentiation grades

Hemoglobin Levels	Histopathological differentiation		Total	p-value
	Low grade	High grade		
Normal	31 20.1%	6 3.9%	37 24.0%	0.822
Anemia	94 61.1%	23 14.9%	117 76.0%	
Total	125 81.2%	29 18.8%	154 100%	

Table 4 shows increased NLR in the low-grade group (75 individuals, 48.7%) and the high-grade group (21 individuals, 13.6%). The normal NLR group consists of 50 low-grade patients (32.5%) and 8 high-grade patients (5.2%). The chi-square test yielded a p-value of 0.303 (p>0.05). These data indicate no significant relationship between NLR values and CRC histopathological differentiation grade.

Table 4. Association between neutrophil to lymphocyte Ratio values and histopathological differentiation grades

NLR Values	Histopathological differentiation		Total	*p* value
	Low grade	High grade		
Normal	50 32.5%	8 5.2%	58 37.7%	0.303
Elevated	75 48.7%	21 13.6%	96 62.3%	
Total	125 81.2%	29 18.8%	154 100%	

DISCUSSION

Research conducted by Sutrisno et al. reported that the majority of CRC patients were male (58.97%) in several studies (Sutrisno et al., 2025). Sung et al. in GLOBOCAN estimated an increase in CRC risk with age, reaching 1.9 million new cases by 2040 (Sung et al., 2021). Research at Ibnu Sina Hospital, Makassar, found the highest incidence in the 46-55 year age group (38.2%) (Husnah et al., 2024). A study at Abdul Moeloek Hospital identified nutritional status as a significant risk factor, with a predominance of underweight patients (BMI<18.5kg/m2; 43.6%) (Widya et al., 2023). Ramadhan et al. associated smoking habits with the incidence of CRC in Lampung, which reached 66.7% (Ramadhan, 2024). The findings of patients aged over 50 years (62.3%) in this study support the conventional carcinogenesis theory and GLOBOCAN data (Husnah et al., 2024; Sung et al., 2021). This research data showed a dominance of female patients (55.8%), which differs from previous studies (Siegel et al., 2022; Sutrisno et al., 2025). The proportion of normal BMI (44.8%) in this study differs from other studies, which show dominance of underweight or overweight (Husnah et al., 2024; Ramadhan, 2024). The high rate of non-smoking patients (60.4%) differs from the findings of Sawicki et al. regarding the role of smoking in Western countries (Sawicki et al., 2021). This phenomenon likely correlates with the high proportion of female subjects, considering that the prevalence of male smoking is higher in Indonesia.

Research conducted by Rudiman et al. at Dr. Hasan Sadikin Hospital, Bandung, found that the most frequently encountered histological type was well differentiated (58.3%), followed by moderate (36.1%) and poor (5.6%). Rudiman also reported a statistically significant correlation (p = 0.004) between tumor cell differentiation and CEA levels, with patients with well-differentiated tumors showing a higher mean CEA level (138.18ng/mL) than those with poorly differentiated tumors (1.55 ng/mL). The existence of this significant relationship can be explained by a pathophysiological mechanism in which high CEA levels in low-grade tumors result from cells that retain adhesion properties, thereby maintaining their capacity to produce the CEA glycoprotein. Conversely, poor differentiation causes cancer cells to lose the ability to express CEA effectively, even though the tumor is aggressive. The results of the comparison between this research and previous studies are consistent with those of Rudiman et al., indicating that a high proportion of low-grade groups exhibit increased CEA levels (Rudiman et al., 2021).

The finding of a high prevalence of anemia in this low-grade differentiation group is consistent with a study conducted by Simatupang et al. at H. Adam Malik Hospital, reporting that 83% of CRC patients experience anemia, generally caused by chronic gastrointestinal bleeding due to tumor infiltration and systemic inflammation that inhibits erythropoiesis (Simatupang et al., 2025). Rajabto et al. emphasized that iron deficiency anemia is a primary clinical manifestation of CRC, especially in right-sided tumor locations, due to long-term occult bleeding (Rajabto et al., 2021). The results of this study have a strong correlation with the research by Simatupang et al.

regarding the high incidence of anemia in CRC patients in Indonesia (Simatupang et al., 2025). Although no statistically significant relationship was found, the dominance of low-grade patients with anemia (61.1%) in this study reflects the sample population, which is indeed composed primarily of low-grade cases. This explains that the impact caused by each tumor differentiation in CRC will reflect a significant clinical manifestation, namely anemia, as a result of a combination of tumor bleeding and chronic systemic inflammation occurring at all degrees of cellular malignancy.

Allahyari et al. reported that patients with advanced disease had a median NLR of 4.8, which was significantly associated with progressive disease post-therapy (Allahyari et al., 2025). The dominance of low-grade differentiation is in line with data from Lukman et al. in West Java, who found that 98.5% of cases were adenocarcinoma NOS, which are generally well to moderately differentiated (Lukman et al., 2024). The high proportion of patients with low-grade differentiation and increased NLR values (48.7%) illustrates that even though tumor cells have better differentiation, the systemic inflammatory response still occurs significantly; it can be concluded that NLR can be used as a marker for systemic inflammation in CRC, but it does not have a significant linear correlation to predict the degree of histopathological differentiation.

CONCLUSION

Based on the research results and discussion, it can be concluded that there is a statistically significant relationship between Carcinoembryonic Antigen (CEA) levels and histopathological differentiation in colorectal cancer patients, with high CEA levels more commonly observed in the low-grade differentiation group. This indicates that CEA can serve as a potential indicator of tumor cell differentiation. Conversely, this study did not find a significant relationship between hemoglobin levels or Neutrophil to Lymphocyte Ratio (NLR) values and the degree of histopathological differentiation. Although anemia and elevated NLR values were widely observed in the research subjects, these conditions are common clinical manifestations of chronic bleeding and systemic inflammatory responses in colorectal malignancy. However, they do not specifically reflect the degree of cell differentiation.

AUTHOR'S DECLARATION

Authors' contributions and responsibilities

MZI: Writing original draft, visualization, funding acquisition, conceptualization; **DY:** writing original draft (supporting), supervision; **AS:** original draft (supporting), supervision; **WAH, R, EN:** review, editing, finishing manuscript

Availability of data and materials

All data are available from the authors.

Competing interests

The authors declare no competing interests.

REFERENCES

Aden, K. A. T., Mulyani, H., Suchitra, A., Hilbertina, N., & Nurhayati, N. (2025). Analisis Karakteristik Klinikopatologi Kanker Kolorektal di Laboratorium Patologi Anatomi RSUP Dr. M. Djamil 2020-2022. *Jurnal Penelitian Sains*, *27*(1), 1. https://doi.org/10.56064/jps.v27i1.1181

Allahyari, A., Fallah, F., Bahrami Taqanaki, P., Pouria Tafti, S., Vakilzadeh, M. M., Moeini Nodeh, M., Kamandi, M., & Noferesti, A. (2025). Evaluating the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) as prognostic and treatment response biomarkers in stage IV colorectal cancer patients. *Oncology in Clinical Practice*, *21*(3), 200–205. https://doi.org/10.5603/ocp.99934

Asprilia R, Efrida, & Syofiati. (2024). Differences in Carcinoembryonic Antigen (CEA) Levels Based on the Degree of Histopathological Differentiation of Colorectal Cancer: Single Center Observational Study at Dr. M. Djamil General Hospital, Padang, Indonesia. *Bioscientia Medicina : Journal of Biomedicine and Translational Research*, *8*(8), 4789–4795. https://doi.org/10.37275/bsm.v8i8.1054

Gvirtzman, R., Livovsky, D. M., Tahover, E., Goldin, E., & Koslowsky, B. (2021). Anemia can predict the prognosis of colorectal cancer in the pre-operative stage: a retrospective analysis. *World Journal of Surgical Oncology*, *19*(1). https://doi.org/10.1186/s12957-021-02452-7

Hamid, H. K. S., Davis, G. N., Trejo-Avila, M., Igwe, P. O., & García-Marín, A. (2021). Prognostic and predictive value of neutrophil-to-lymphocyte ratio after curative rectal cancer resection: A systematic review and meta-analysis. In *Surgical Oncology* (Vol. 37). Elsevier Ltd. https://doi.org/10.1016/j.suronc.2021.101556

Hasan MF, Hilbertina N, & Deddy S. (2022). Clinicopathological Characteristics of Colorectal Cancer in the Anatomical Pathology Laboratory of Dr. M. Djamil Padang General Hospital, 2017-2020. *Repositori Universitas Andalas*, 27–36. https://doi.org/http://scholar.unand.ac.id/id/eprint/100410

Husnah A, Yanti AK, Arifin AF, Hasbi BE, & Ikram D. (2024). Characteristics of Colorectal Cancer Patients at Ibnu Sina Teaching Hospital, Makassar, in 2022. *Jurnal Ilmu Kedokteran dan Kesehatan*, 19–28. https://doi.org/https://fmj.fk.umi.ac.id/index.php/fmj/article/view/435/258

Iskandar, M., Tendean, M., Salem, B., & Langi, F. G. (2023). Correlation between Neutrophil-to-Lymphocyte Ratio and Pre-Postoperative Carcinoembryonic Antigen Levels in Colorectal Cancer. *Medical Scope Journal*, *5*(2), 270–278. https://doi.org/10.35790/msj.v5i2.46621

Joseph L, Anthony F, Dennis K, Stephen H, Longo, & J.Larry J. (2022). Harrison's Principles of Internal Medicine, Twenty-First Edition. In *Harrison's Principles of Internal Medicine* (21st ed., Vol. 1). McGraw-Hill Education/Medical.

Kankanala, V. L., Zubair, M., & Mukkamalla, S. K. R. (2024). Carcinoembryonic Antigen. *StatPearls*. https://www.ncbi.nlm.nih.gov/books/NBK578172/

Lukman, K., Muhammad, A., Ghozali, M., Nugraha, P., Sribudiani, Y., & Nursabur, B. M. (2024). Epidemiological and Clinicopathological Characteristics of Colorectal Cancer Patients in a Tertiary Hospital in West Java. *Clinical Epidemiology and Global Health*, *28*. https://doi.org/10.1016/j.cegh.2024.101688

Mohammad, F., Muhar, A. M., & Siregar, E. S. (2024). Association Between Recurrence Rates of Colorectal Cancer and Carcinoembryonic Antigen Levels, Histopathological Features, Tumor-Infiltrating Lymphocytes, and Lymphatic Invasion at H. Adam Malik Central General Hospital, Medan. *The Indonesian Journal of General Medicine*, *4*, 40–55. https://doi.org/https://doi.org/10.70070/eqs5ry48

Purnomo, H., Handaya, Y., & Setyawan, N. (2024). Neutrophil to Hemoglobin Lymphocyte Ratio (NHLR) as a Novel Biomarker is Superior to Neutrophil Lymphocyte Ratio (NLR) and Platelet Lymphocyte Ratio (PLR) as Predictors of Advanced Colorectal Cancer. *Indonesian Journal of Cancer*, *18*(1), 47–52. https://doi.org/10.33371/ijoc.v18i1.1099

Rajabto, W., Tridana Sakti, P., & Putra Kevinsyah, A. (2021). Iron Deficiency Anemia as The Only Manifestation of Colon Cancer in a Male Patient: A Case Report. *The Indonesian Journal of Gastroenterology, Hepatology, and Digestive Endoscopy*, *21*(3). https://doi.org/10.24871/2132020241-243

Ramadhan, R. S. (2024). Positive Correlation between Tumor-Associated Macrophages and Clinical Stage in Colorectal Adenocarcinoma. *Majalah Kedokteran Andalas*, *46*(3), 578–591. https://doi.org/10.25077/mka.v46.i4.p578-591.2023

Rudiman, R., Lukman, K., & Barr, T. I. (2021). Correlation Between Tumor Cell Differentiation and CEA Levels in Patients with Adenocarcinoma of the Rectum. *Majalah Kedokteran Bandung*, *52*(4). https://doi.org/10.15395/mkb.v52n4.2028

Sawicki, T., Ruszkowska, M., Danielewicz, A., Niedźwiedzka, E., Arłukowicz, T., & Przybyłowicz, K. E. (2021). A review of colorectal cancer in terms of epidemiology, risk factors, development, symptoms, and diagnosis. In *Cancers* (Vol. 13, Issue 9). https://doi.org/10.3390/cancers13092025

Shabo, I., Nordling, E., & Abraham-Nordling, M. (2025). Artificial intelligence prediction of carcinoembryonic antigen structure and interactions relevant for colorectal cancer. *Biochemistry and Biophysics Reports*, *42*. https://doi.org/10.1016/j.bbrep.2025.102024

Siegel, R. L., Miller, K. D., Fuchs, H. E., & Jemal, A. (2022). Cancer statistics, 2022. *CA: A Cancer Journal for Clinicians*, *72*(1), 7–33. https://doi.org/10.3322/caac.21708

Simatupang, R. V., Katharine, S., B. Y. M., & Abdillah, H. Z. (2025). Hemoglobin Profile, Platelets, and Neutrophil-Lymphocyte Ratio in Colorectal Cancer Patients: A Descriptive Study at Haji Adam Malik General Hospital, Medan. *Jurnal Kedokteran Meditek*, *31*(5). https://doi.org/10.36452/jkdoktmeditek.v31i5.3488

Sung, H., Ferlay, J., Siegel, R. L., Laversanne, M., Soerjomataram, I., Jemal, A., & Bray, F. (2021). Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA: A Cancer Journal for Clinicians*, *71*(3), 209–249. https://doi.org/10.3322/caac.21660

Sutrisno, Jennah AY, & Puspita EA. (2025). The Relationship Between Age and Gender with Colorectal Cancer Stage at Dr. Soegiri Lamongan Regional Hospital. *Jurnal Medis Umum*, *2*, 38–48. https://doi.org/10.30651/jmu.v2i1.25637

Widya A, Siswandi A, Wulandari M, & Kumala I. (2023). Characteristics of stage I-IV colorectal cancer patients at Dr. H. Abdul Moeloek Regional General Hospital. *Jurnal Ilmu Kedokteran dan Kesehatan*, *10*(7), 2360–2374. https://doi.org/10.33024/jikk.v10i7.10805