Original Article

Diagnostic and Prognostic Utility of Lymphocyte-to-Monocyte Ratio and Hemoglobin-to-Platelet Ratio in Colorectal Cancer: A Cross-Sectional Study in Iraq

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Abstract

Background: Colorectal cancer (CRC) is a major global health burden, the third most common cancer, and the second leading cause of cancer-related deaths. Chronic inflammation is the key driver of its pathogenesis. Although colonoscopy is the diagnostic gold standard, its limitations necessitate the use of noninvasive biomarkers. Inflammation-based ratios, such as the Lymphocyte-to-Monocyte Ratio (LMR) and Hemoglobin-to-Platelet Ratio (HPR), are derived from routine blood tests. **Objective:** This study evaluated the diagnostic value of LMR and HPR, both individually and in combination, for early detection of CRC in an Iraqi cohort. We further assessed their association with histopathological tumor features (tumor stage, grade, lymph node involvement, and metastasis) and disease stage. **Materials and Methods:** A cross-sectional study was conducted from September 2024 to April 2025, involving 60 newly diagnosed, treatment-naive CRC patients (stages I-IV) from hospitals in Hilla, Karbala, and Al-Najaf, Iraq. Patients with significant comorbidities, prior anti-cancer treatment, or recent transfusions were excluded. Complete Blood Count (CBC) analysis (using ADVIA 2120i) was used to calculate LMR and HPR. Associations with clinicopathological features were analyzed using t-tests, ROC analysis, and multivariate regression. **Results:** Decreased LMR and HPR were significantly associated with advanced disease. Lower LMR was correlated with lymph node metastasis (N0 vs. N+: p=0.03) and advanced clinical stage (I/II vs. III/IV, p=0.037). Lower HPR was correlated with deeper tumor invasion (T1+T2 vs. T3+T4: p=0.046), lymph node metastasis (N0 vs. N+: p=0.04), advanced clinical stage (I/II vs. III/IV: p=0.0033), and distant metastasis (M0 vs. M1, p=0.005). ROC analysis showed that HPR had a higher diagnostic accuracy for distinguishing early (I/II) from advanced (III/IV) stages (AUC=77%, sensitivity =65%, specificity =88% at cut-off >0.5) than LMR (AUC=65%, sensitivity =84% at cut-off >3.3). Multivariate regression confirmed that LMR (β=−0.43, p=0.016) and HPR (β=−4.94, p=0.005) were significant independent inverse predictors of advanced-stage disease. Conclusion: This study revealed that LMR and HPR are readily accessible, low-cost inflammatory biomarkers inversely associated with advanced colorectal cancer progression in Iraqi patients. Decreased levels of both ratios, particularly HPR, correlated significantly with adverse histopathological features (lymph node metastasis, deeper invasion, advanced TNM stage, distant metastasis) and demonstrated moderate diagnostic utility for identifying advanced disease.

Keyword: Colorectal cancer, Lymphocyte-to-monocyte ratio, Hemoglobin-to-platelet ratio, Biomarkers, Prognosis, Inflammation

Introduction

Colorectal cancer (CRC) has emerged as a significant global health concern, with its incidence showing a marked increase coinciding with the deterioration of lifestyle and dietary patterns[1]. Recognized as the third most prevalent malignancy worldwide and the second leading cause of cancer-related mortality, CRC was estimated to affect approximately 1.9 million individuals and cause 0.9 million deaths globally in 2020[2]. The epidemiological distribution of CRC demonstrates considerable

variation across different countries, with higher prevalence rates observed in developed nations than in low- and middle-income countries. However, the incidence is progressively increasing in developing countries due to westernization and environmental factor modifications, with projections indicating a 60% increase by 2030 [3–5]. CRC is the third most common malignancy in Iraq, with 2,328 new cases documented in 2019 [6, 7]. The overall CRC incidence proportion increased from 2.28 to 6.18 per 100,000 population between 2000 and 2019, representing an annual percentage change of 5.11%[8]. Similar to other developing nations, CRC cases in Iraq have shown significant increases across both sexes since 2007[9]. The demographic profile reveals that cancer incidence is closely associated with aging, with the majority of CRC cases occurring after the age of 50 years. Males demonstrate higher susceptibility than females, potentially due to greater exposure to environmental factors[10]. The pathogenesis of CRC involves multiple risk factors categorized into modifiable factors (including dietary habits and lifestyle choices) and non-modifiable factors (such as age, sex, and ethnicity), which frequently co-occur and interact to promote CRC development[11]. Genetic factors contribute significantly to CRC pathogenesis primarily through proto-oncogene activation or tumor suppressor gene inactivation [12]. Adenocarcinoma, originating from glandular epithelial cells of the colon and rectum, accounts for over 90% of CRC cases, whereas other histological types include squamous cell carcinoma[13], adenosquamous carcinoma, and undifferentiated carcinoma. Based on mutational origins, CRC can be classified as sporadic (70% of cases without a family history), familial (25% with a family history), or inherited (5% due to hereditary cancer syndromes such as familial adenomatous polyposis and Lynch syndrome) [14]. The molecular pathogenesis of CRC occurs via three primary mechanisms: microsatellite instability, chromosomal instability, and cytosine guanine (CpG) island methylator phenotype[12]. Chronic inflammation plays a pivotal role in CRC pathogenesis, indicating that inflammatory biomarkers may possess diagnostic utility for this malignancy[15]. As one of the most prevalent malignancies globally, CRC has stimulated extensive research into novel biomarkers owing to its high incidence and clinical burden[16]. Recent investigations have emphasized the critical contribution of inflammatory cells and mediators within the tumor microenvironment to CRC progression. The malignant phenotype stimulates inflammatory cells, resulting in changes to cellular immunity and prompting these cells to generate soluble factors such as cytokines and other inflammatory mediators[17]. The lymphocyte-to-monocyte ratio (LMR) is an inflammation-based biomarker with significant prognostic value in patients with CRC [18]. Lymphocytes are small white blood cells that play crucial roles in adaptive immunity, whereas monocytes are large white blood cells that are involved in innate immunity and inflammatory responses. The LMR reflects the balance between adaptive immune responses and inflammatory processes within the tumor microenvironment[19]. The hemoglobin-platelet ratio (HPR) has emerged as another promising inflammatory biomarker for CRC diagnosis and prognosis[20]. This ratio reflects the balance between anemia (often present in CRC due to gastrointestinal bleeding) and thrombocytosis (commonly associated with inflammatory responses and malignancy) [21]. Despite the established prognostic value of individual inflammatory biomarkers such as

LMR and HPR in CRC, significant research gaps persist, including limited evidence on their combined diagnostic utility, insufficient exploration of their association with histopathological tumor features (e.g., invasion depth, lymph node metastasis, and TNM stage) in Iraqi populations, and a lack of validation of these accessible, low-cost biomarkers as tools for early CRC detection in resource-constrained settings[20, 21]. This study aimed to evaluate the diagnostic efficacy of LM) and HPR, individually and in combination, for early detection of CRC in an Iraqi cohort, and to assess their correlations with histopathological tumor features (tumor stage, grade, lymph node involvement, metastasis) and disease progression.

Materials and Methods

Study design

This cross-sectional study was conducted from September 2024 to April 2025, across multiple sites in Iraq. The participating centers included Alemam Alsadeq Teaching Hospital, AL-Hilla Teaching Hospital, and governmental/private hospitals and clinics in Hilla, Karbala, and Alnagaf. Sixty patients (CRC) patients attending oncology outpatient clinics at these facilities were enrolled in the study.

Participant Eligibility Criteria

Eligible participants were patients with newly diagnosed CRC (stages I–IV), confirmed via clinical and histopathological reports from governmental or private sectors. Key exclusion criteria were (1) concurrent infections, hematological disorders, cardiovascular/cerebro-vascular diseases, systemic illnesses, or additional malignancies; (2) prior receipt of pre-surgical anticancer therapies (chemotherapy/ radiotherapy); and (3) recent blood transfusions. All enrolled patients underwent standardized assessment and tumor staging according to the American Joint Committee on Cancer (AJCC) staging system[22].

Biomarker Analysis

Two milliliters of whole blood were collected from each participant into EDTA anticoagulant tubes (concentration: 1.2 mg EDTA per 1 mL blood). Samples were designated for complete blood count (CBC) analysis and subsequent calculation of the LMR and HPR. CBC testing was centralized at the Marjan Teaching Hospital to ensure methodological consistency. CBC parameters were quantified using an automated hematology system (Siemens ADVIA 2120i). Whole blood samples in EDTA tubes were processed within one hour of collection to maintain analytical precision. Strict adherence to the one-hour processing window minimized pre-analytical variability and guaranteed the reliable measurement of hematological biomarkers.

Statistical analysis

All statistical analyses were performed using GraphPad Prism version 9. Data were initially collated in Microsoft Excel, coded, and transferred to the GraphPad software for processing. Descriptive statistics included mean ± standard deviation (SD), median, interquartile range (IQR), and percentage for categorical variables. Inferential analyses were conducted as follows. Chi-square tests assessed associations between categorical variables (e.g., tumor site distribution). Independent sample t-tests compared continuous variables between subgroups (e.g., tumor site subgroups). Receiver operating characteristic (ROC) curve analysis was used to determine the sensitivity, specificity, and area under the curve (AUC) for biomarkers (LMR and HPR) in distinguishing between early and advanced stages. Stepwise multiple

regression was used to identify predictors of advanced disease (clinical stage). Variables with $p < 0.05$ were retained in the final model. The Variance Inflation Factor (VIF < 5) confirmed the absence of multicollinearity. Statistical significance was set at $p < 0.05$.

Ethical considerations

All patients received verbal information explaining the aims of the study. Verbal consent was obtained from all the patients participating in the study. Ethical approval for the study was obtained from the ethical committee of the Department of Pathology and Council of the College of Medicine/University of Babylon.

Results

The results section begins by outlining the demographic and clinical characteristics of the cross-sectional study, including age, sex distribution, tumor site, and tumor size. Subsequent analyses delve into pathological classifications such as tumor stage, grade, lymph node involvement, and metastasis status, which are pivotal in determining disease progression and management strategies. Furthermore, the study evaluated hematological biomarkers, LMR, HPR, and neutrophils, to assess their variability across clinical stages and diagnostic performance in distinguishing early from advanced disease.

Table 1: Baseline Characteristics of Colorectal Cancer Patients

Characteristic		Mean ±SD / No.	Range/ %
Age (years)		54.07 ± 14.66	26 - 81
Gender	Male	36	(60%)
	Female	24	(40%)
Tumor Site	Sigmoid	14	(23%)
	Rectum	18	(30%)
	Other	28	(47%)
Tumor Size (cm)		4.64 ± 1.8	1 - 10

This table details tumor staging (30% Stage IV, 25% Stage III), Grade II (70%), lymph node involvement (58% N0), and metastasis status (67% M0). Tumor invasion categories (T1–T4) were also reported, with T3 being the most prevalent (46%).

Table 2: Pathological Staging and Grading of Colorectal Cancer Patients

Characteristic		No.	Range/ %
Tumor Stage	I	13	22%
	II	14	23%
	III	15	25%
	IV	18	30%
Tumor Grade	I	11	18%
	II	42	70%
	III	7	12%
Tumor /Invasion	T I	6	12%
	T II	14	30%
	T III	22	46%
	T IV	6	12%
Lymph Node	N 0	35	58%
	N I	13	22%
	N II	12	20%
Metastasis	M 0	40	67%
	M I	20	33%

The majority of patients (42%) were aged 61–81 years, followed by 41–60 years (35%), and 21–40 years (23%). This finding highlights the higher incidence of CRC in the older population.

Table 3: Age Group Distribution of Colorectal Cancer Patients

Age groups	Colorectal cancer n = 60
21-40 Years	14 (23)%
41-60 Years	21 (35)%
61-81 Years	25 (42)%
Total	164 (100)%

Table 4 summarizes the descriptive statistics of the hematological biomarkers across the study cohort. White blood cell (WBC) counts ranged from 4.9 to 8.4 x10^9/L, with a mean of 6.88 ±

0.69 x10⁹/L and a median of 6.93 x10⁹/L, indicating a symmetric distribution. Lymphocyte counts exhibited a broader range (0.30–2.90 x10⁹/L) with moderate variability (IQR = 0.7). Monocyte values were comparatively lower (mean: 0.49 ± 0.2 x10⁹/L) and less dispersed (IQR = 0.21). The LMR averaged 3.63 ± 0.79, while hemoglobin levels ranged from 98.9 to 139 g/L (mean: 116 ± 11.85 g/L). Platelet counts showed a mean of 228 ± 32.28 x10⁹/L, and the HPR was 0.51 ± 0.07.

Table 4: Descriptive Statistics of Hematological Biomarkers

Hematological Parameters	Minimum	Maximum	Mean	±SD	Median	IQR
WBC (x109/L)	4.9	8.4	6.88	0.69	6.93	0.9
lymphocytes (x 109/L)	0.30	2.90	1.56	0.44	1.58	0.7
Monocytes (x 109/L)	0.23	1.2	0.49	0.2	0.43	0.21
Lymphocyte monocyte ratio	2.25	5.17	3.37	0.66	3.33	0.932
Hemoglobin	98.9	139	116	11.85	117	19.8
Platelet count (x 109/L)	130	300	228	32.28	225	44
Hemoglobin platelet ratio	0.39	0.76	0.51	0.07	0.5	0.08

Table 5 presents associations between inflammatory biomarkers (LMR and HPR) and pathological features in CRC. Lymph node metastasis-negative (N0) patients exhibited significantly higher LMR (mean ± SD: 3.51 ± 0.68 vs. 3.1 ± 0.6; p = 0.03) and HPR (0.52 ± 0.069 vs. 0.48 ± 0.068; p = 0.04) compared to N+ cases. Advanced clinical stages (III/IV) correlated with reduced LMR (3.2 ± 0.54 vs. 3.62 ± 0.8; p = 0.037) and HPR (0.48 ± 0.062 vs. 0.54 ± 0.072; p = 0.0033) relative to early stages (I/II). Distant metastasis (M1) was associated with lower HPR (0.47 ± 0.049 vs. 0.52 ± 0.073; p = 0.005) but not LMR (p = 0.2). HPR was also lower in T3+T4 tumors (0.53 ± 0.07) versus T1+T2 (0.49 ± 0.062; p = 0.046), while tumor size (>5 cm vs. ≤5 cm) showed no significant differences for either biomarker (p > 0.5).

Table 5: Association of Inflammatory with Tumor Staging and Metastasis in in Colorectal Cancer

	No.	LMR	*P*	HPR	*P*
Tumor/ Invasion					
T1+T2	**20**	3.4 ± 0.68	0.2	0.49 ± 0.062	0.046*
T3+T4	**28**	3.3 ± 0.64		0.53 ± 0.07	
lymph nodes metastasis					
NO	**35**	3.51 ± 0.68	0.03*	0.52 ± 0.069	0.04*
YES	**25**	3.1 ± 0.6		0.48 ± 0.068	
Clinical Stage					
I/II	**27**	3.62 ± 0.8	0.037*	0.54 ± 0.072	0.003**
III/IV	**33**	3.2 ± 0.54		0.48 ± 0.062	
Distant metastasis (M stage)					
M0	**40**	3.4 ± 0.68	0.2	0.52 ± 0.073	0.005**
M1	**20**	3.2 ± 0.61		0.47 ± 0.049	
Tumor Size (cm)					
< 5	**31**	3.38 ± 0.6	0.9	0.51 ± 0.075	0.5
> 5	**29**	3.37 ± 0.73		0.5 ± 0.065	

The diagnostic efficacy of LMR and HPR in distinguishing early stage (I/II) from advanced-stage (III/IV) CRC was assessed using receiver operating characteristic (ROC) curve analysis. The HPR exhibited moderate diagnostic accuracy (AUC: 77%; sensitivity: 65%; specificity: 88%) at a threshold of >0.5. The LMR showed a lower discriminative capacity (AUC: 65%) but high sensitivity (84%) at a cut-off of >3.3. The positive and negative predictive values ranged from 73% to 88% and 73% to 100%, respectively.

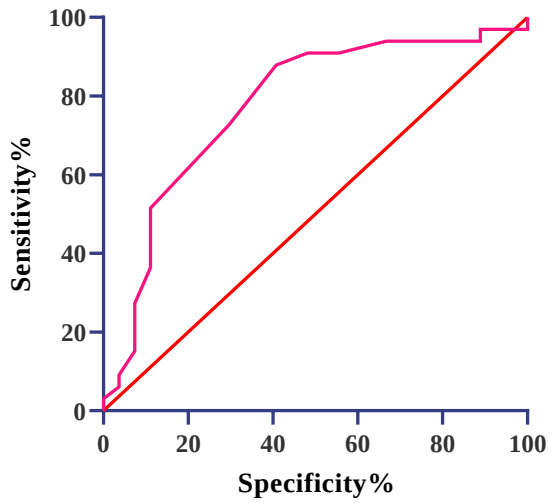

Figure 1: ROC Curve Analysis for Hemoglobin-Platelet Ratio in Differentiating Early vs. Advanced Colorectal Cancer

Table 6 displays the outcomes of stepwise multiple regression analysis conducted to identify significant predictors of advanced clinical stage. The final model retained two independent variables, HPR and LMR, while WBC was excluded due to non-significance. The LMR (B = -0.43, SE = 0.17, t = -2.48, p = 0.016) and HPR (B = -4.94, SE = 1.69, t = -2.91, p = 0.005) showed significant negative associations. The model accounted for 43% of the variance in the clinical stage (R^2 = 0.43) and was statistically significant (F-ratio = 13.16, p < 0.0001), with a moderate multiple correlation coefficient (R = 0.66). The Variance Inflation Factor (VIF = 1.06) confirmed the absence of substantial multicollinearity among the predictors.

Table 6: Multiple Regression Analysis of Advanced Clinical Stage with Stepwise Selection

Clinical Stage	Dependent variable			
Independent variables in the model	B (Coefficient)	Std. Error	t-value	P. Value
LMR	- 0.43	0.17	- 2.48	0.016
HPR	- 4.94	1.69	- 2.91	0.005
WBC	Non-significant in the model			
Variance Inflation Factor	1.06			
Model (R^2 = 0.43) F-ratio (13.16) The model is statistically significant (P < 0.0001). Multiple correlation coefficient (R 0.66)				

B (coef): Regression Coefficient; CI: Confidence Interval

Table 7 compares the clinical variables between the CRC subgroups stratified by tumor site (colon, n = 42; rectum, n = 18). Mean values for WBC, LMR, and HPR were analyzed using independent sample t-tests. A statistically significant difference was observed in LMR, with rectal tumors exhibiting higher mean values compared to colon tumors (4.0 ± 0.8 vs. 3.4 ± 0.75, p = 0.018). No significant differences were found in WBC (6.7 ± 0.72 vs. 6.9 ± 0.67, p = 0.2), HPR (0.5 ± 0.06 vs. 0.5 ± 0.07, p = 0.9).

Table 7: Subgroup Analysis Based on Tumor Site [Groups: Colon (e.g., sigmoid, rectum, cecum) vs. Rectum.]

Study variables		Colorectal Cancer (Tumor Site)		P-value
		Colon(42)	Rectum (18)	
WBC ($x10^9$/L)	Mean ±SD	6.9 ± 0.67	6.7 ± 0.72	0.2
LMR		3.4 ± 0.75	4.0 ± 0.8	0.018*

HPR		0.5 ± 0.07	0.5 ± 0.06	0.9
NGAL		69.9 ± 4.6	68.9 ± 6.1	0.4

I: independent samples t-test; NS: not significant ($p \geq 0.05$).

Discussion

Colorectal cancer (CRC) is a significant global health burden, underscoring the critical need for timely diagnosis. Although colonoscopy remains the diagnostic gold standard, its inherent invasiveness, procedural risks, and substantial cost limit its utility for widespread routine screening [23]. Consequently, there is a compelling clinical imperative to identify faster, less invasive, and more accurate diagnostic biomarkers. Chronic inflammation is a well-established driver of tumorigenesis, and hematological inflammatory indices, such as LMR and HPR, have demonstrated diagnostic and prognostic utility in various malignancies. Nevertheless, the combined clinical value of these markers in CRC surveillance remains inadequately characterized [24]. In this study, key sociodemographic, lifestyle, and clinical characteristics were adjusted in the analyses. Consistent with established epidemiology [25, 26], CRC incidence was markedly lower in younger age groups than in older individuals (mean age, 54 years). Most cases (42.0%) occurred within the 61–81-year age bracket, reinforcing the strong association between advancing age and CRC risk. This finding aligns with the existing literature [25, 26] and highlights the necessity for robust age-targeted screening initiatives. A male predominance was observed (60% male vs. 40% female), corroborating the sex distribution patterns reported in prior studies [27]. Regarding tumor localization, the rectum was the single most frequent primary site (30%), while other colonic segments collectively accounted for 70% of the cases. The sigmoid colon was the most common site (23%) [28]. Analysis of histopathological features revealed moderately differentiated adenocarcinoma as the predominant subtype (70%), consistent with previous reports [29]. In terms of TNM staging, Stage IV disease was the most prevalent at diagnosis, mirroring recent epidemiological trends [30]. Further stratification showed that T3 was the most frequent primary tumor depth (46%), consistent with prior observations [30]. Lymph node involvement analysis indicated that 58% of patients were node-negative (N0) at presentation, a distribution noted in comparable cohorts[23]. Hematological parameters in peripheral blood represent a simple, reproducible, and widely accessible method for prognostic evaluation in oncology, particularly within the Chinese healthcare system where they provide valuable reference data across diverse hospital tiers by Chen et al., (2020) [31]. Such parameters have been established as reliable paraclinical tools for disease diagnosis, predicting severity, mortality, and informing treatment strategies for breast cancer. In the present study of CRC patients, a significant reduction in hemoglobin levels (mean: 10.98 g/dL) was observed. This finding aligns with previous reports on breast cancer, where decreased mean values of RBC, Hb, HCT, MCV, and MCH were documented relative to healthy controls. However, divergent patterns were observed for other parameters. Our CRC cohort exhibited platelet and total WBC counts within the normal ranges. In contrast, lymphocyte and monocyte counts were either within the lower limit of normal or decreased. This profile differs from the elevated WBC count reported for breast cancer [29].. The observed lymphopenia in our CRC patients is consistent with findings in testicular cancer, where similarly reduced lymphocyte counts occurred despite elevated total WBC counts by Çalışkan

et al. (2017) [32]. The study findings demonstrated a significantly lower LMR in patients with CRC, consistent with prior research. Consistent with the report by Li et al. [33], who observed significantly decreased LMR in CRC patients versus those with benign tumors, our results further support the potential utility of LMR as a predictor of CRC. Li et al. additionally associated a higher pre-operative LMR with favorable clinicopathological characteristics, including reduced depth of invasion, less frequent lymph node metastasis, earlier tumor stage, and smaller tumor size. While our study did not find statistically significant associations between LMR and tumor invasion depth, size, or distant metastasis, it showed significant inverse correlations with lymph node involvement and advanced clinical stage (Stage IV exhibiting the lowest LMR). The prognostic relevance of the LMR in CRC is further underscored by its correlation with overall survival (OS). A low pre-treatment LMR has been established as an indicator of poorer OS in CRC patients [34], a finding corroborated by Kozak et al., who identified a declining LMR as an independent predictor of worse OS [34]. Regarding diagnostic performance, study evaluation revealed that decreasing the LMR significantly predicted CRC presence in the study cohort, yielding an area under the curve (AUC) of 0.65. Although this indicates a moderate discriminative capacity, LMR demonstrated high sensitivity (84%) at a cutoff value of >3.3, consistent with previous findings [34]. To enhance the diagnostic or predictive efficacy, we investigated the LMR within the combined biomarker models. Logistic regression analyses revealed that the LMR was significantly associated with the likelihood of CRC detection. Importantly, integrating the LMR with other hematological markers (discussed subsequently) significantly improved the ability to identify CRC cases. This synergistic effect aligns with findings from other studies [14, 35], suggesting that LMR, particularly in combination panels, enhance diagnostic utility. For instance, Mo et al. [14] reported increased diagnostic efficacy of LMR in rectal cancer, while Jakubowska et al. (2020) identified postoperative LMR as an independent prognostic factor in CRC [35]. The observed associations between low LMR and the adverse pathological features of CRC can be interpreted mechanistically. Lymphocytes are critical mediators of antitumor immunity, inhibiting proliferation and metastasis through tumor antigen recognition, direct cytolysis, and cytokine release. Consequently, lymphocyte-penia may compromise immune surveillance and attenuate lymphocyte-dependent antitumor responses, thereby facilitating disease prog-ression. Conversely, monocytes, key components of the mononuclear phagocyte system, are pivotal regulators of cancer development. Within the tumor microenvironment, factors secreted by malignant cells can drive monocyte differentia-tion into tumor-associated macrophages (TAMs). These TAMs often exhibit pro-tumorigenic functions, promoting tumor initiation and progression via the production of factors, such as reactive oxygen species and fibroblast growth factor [24]. Extensive meta-analyses have established the prognostic significance of LMR in CRC. A comprehensive meta-analysis involving 11,783 patients from 15 retrospective studies demonstrated that elevated LMR was associated with significantly improved overall survival (hazard ratio = 0.57, 95% confidence interval: 0.52-0.62, $P < 0.001$), disease-free survival (hazard ratio = 0.77, 95% confidence interval: 0.70-0.84, $P < 0.001$), and cancer-specific survival (hazard ratio = 0.55, 95% confidence interval: 0.32-0.95, $P = 0.031$).

Additionally, an increased LMR was significantly associated with tumor invasion depth and tumor size [36]. In metastatic CRC, recent systematic reviews by Mei et al. (2025) confirmed the prognostic utility of LMR. A meta-analysis of 14 studies involving 3,089 patients demonstrated that a high LMR correlated with better overall survival (HR: 0.55, 95% CI: 0.49-0.62, p<0.00001), progression-free survival (HR: 0.68, 95% CI: 0.57-0.81, p<0.0001), and cancer-specific survival (HR: 0.55, 95% CI: 0.32-0.95, p=0.03)[37]. The mechanism underlying the prognostic significance of LMRs is related to the immune system's response to malignancy. Low lymphocyte levels indicate weakened immune responses, whereas elevated monocyte counts suggest increased tumor burden and inflammatory activity[38]. An elevated LMR, therefore, indicates robust immune responses (high lymphocytes) combined with reduced inflammatory burden (low monocytes), creating a favorable prognostic environment[39]. The findings of the study showed significantly lower HPR levels in advanced stages, metastasis, and deeper invasion, but not with tumor size. LMR was not associated with metastasis, aligned with those of Mo et al. (2020), demonstrating that low preoperative HPR is significantly associated with adverse clinicopathological features in CRC, including deeper tumor invasion, lymph node metastasis, advanced clinical stage, and distant metastasis. Notably, no significant association was observed between HPR and tumor size. While prior research established HPR as a predictor of 3-year overall survival in locally advanced nasopharyngeal carcinoma [14], the present study extends its relevance to CRC by linking low HPR to aggressive disease characteristics. ROC curve analysis was performed to evaluate the diagnostic efficacy of the HPR for CRC detection. HPR demonstrated a statistically significant predictive value (AUC = 0.77, $p < 0.001$), with a sensitivity of 65% and specificity of 88%. This robust performance (AUC 0.77) confirmed the clinical utility of HPR as a biomarker for stratifying CRC risk among the study subjects. Although research on HPR in solid malignancies remains limited, our results corroborate the findings of Hu et al. (2020), who similarly reported decreased HPR levels in CRC patients compared with controls[21]. Other studies have also linked HPR to tumor invasion and size, and this association was evident in the present study [20, 21]. Studies have demonstrated that patients with CRC exhibit significantly lower HPR values than patients with benign colorectal diseases and healthy controls[21]. The diagnostic value of HPR has been validated through ROC curve analyses, showing AUC values of 0.64 for HPR alone and improved diagnostic accuracy when combined with other biomarkers. When combined with carcinoembryonic antigen (CEA), HPR achieved enhanced diagnostic performance with an AUC value of 0.814 and a sensitivity of 68.09%[14]. The pathophysiological basis for HPR's diagnostic utility lies in the characteristic changes observed in patients with CRC. Mean hemoglobin levels are typically reduced in patients with CRC, primarily due to chronic gastrointestinal bleeding. Concurrently, platelet counts are often elevated because of ongoing inflammatory processes and the presence of malignancy. This combination results in decreased HPR values, which can serve as diagnostic indicators for CRC [40, 41]. Research has demonstrated significant correlations between HPR and the clinicopathological features of CRC, lower HPR values have been associated with increased tumor invasion depth, lymph node metastasis, advanced TNM staging,

and larger tumor sizes. These associations suggest that HPR not only serves as a diagnostic biomarker, but also provides prognostic information regarding disease severity and progression[20]. Furthermore, logistic regression analysis revealed that HPR alone was significantly associated with the likelihood of CRC detection. Importantly, combining HPR with other hematological markers, specifically LMR, significantly enhanced the predictive accuracy for CRC diagnosis, consistent with prior reports [14, 35]. This synergistic effect may stem from the interrelated pathophysiological roles of hemoglobin and platelets in cancer. Tumor-induced anemia often results from bone marrow suppression, dysregulation of iron metabolism, and inflammatory cytokine activity, which can promote tumor hypoxia, angiogenesis, and genomic instability. Platelets facilitate cancer progression and metastasis via the release of growth and angiogenic factors, which are often activated by tumor-derived agonists. Consequently, composite biomarkers integrating HPR and LMR hold promise for the improved monitoring of CRC progression. The clinical significance of this combined approach lies in its potential to provide accessible and cost-effective screening tools that can be derived from routine complete blood count analyses. These biomarkers offer particular value in resource-limited settings where advanced diagnostic modalities may not be readily available. Furthermore, the non-invasive nature of these tests makes them suitable for large-scale screening programs and longitudinal monitoring of high-risk populations[20]

Conclusion

This study demonstrated that the LMR and HPR serve as significant, readily accessible hematological biomarkers reflecting CRC progression in an Iraqi cohort. Both ratios exhibited significant inverse correlations with the established indicators of disease severity and poor prognosis. Specifically, a decreased LMR was significantly associated with lymph node metastasis and advanced clinical stage. Decreased HPR showed even stronger associations, correlating significantly with deeper tumor invasion, lymph node metastasis, advanced clinical stage, and distant metastasis. These findings underscore the utility of LMR and HPR as valuable and cost-effective indicators of tumor burden, disease progression, and adverse histopathological features in CRC. Their derivation from routine complete blood counts positions them as promising prognostic tools and potential adjuncts for risk stratification and monitoring, particularly within resource-limited healthcare environments, such as Iraq. Future studies should explore their combined use and validate the cut-off values in larger prospective cohorts.

Availability of data and material

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The author declare that they have no competing interests

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Author Contribution

The authors were contributed equally in conceptualized the research, collected data, participated in data analysis and write-up, editing and review.

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