Section: Pathology

Original Research Article

PRETREATMENT MONOCYTE-TO-LYMPHOCYTE RATIO (MLR) AND RED CELL DISTRIBUTION WIDTH (RDW) AS PREDICTORS OF TUMOR GRADE AND FIGO STAGE IN ENDOMETRIAL CARCINOMA

Moin Khan[1], Geeta W. Mukhiya[2], Shaifali Goyal[3], Kaustubh Singh[4]

[1]Junior Resident, Department of Pathology, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India.
[2]Professor and Head, Department of Pathology, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India.
[3]Assistant Professor, Department of Pathology, RVRS Medical College, Bhilwara, Rajasthan, India.
[4]Assistant Professor, Department of Pathology, Government Medical College, Dungarpur, Rajasthan, India.

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Corresponding Author:
Dr. Moin Khan,
Junior Resident, Department of Pathology, Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India.
Email: moinkhan1doctor@gmail.com

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ABSTRACT

Background: Endometrial carcinoma is a leading gynecological malignancy where precise risk stratification is critical for determining therapeutic strategies. Pretreatment inflammatory markers offer non-invasive, accessible prognostic insights. This study evaluates the predictive value of the pretreatment monocyte-to-lymphocyte ratio (MLR) and red cell distribution width (RDW) regarding tumor grade and FIGO stage in patients with endometrial carcinoma.

Materials and Methods: A hospital-based cross-sectional study was conducted evaluating 100 women presenting with abnormal uterine bleeding, comprising 47 benign cases, 12 hyperplasia cases, and 41 histopathologically confirmed endometrial carcinoma cases. Pretreatment complete blood count parameters were analyzed to compute MLR and evaluate RDW across different histopathological types, tumor grades, and FIGO stages.

Results: Pretreatment MLR and RDW demonstrated significant progressive increases from benign lesions to carcinoma (0.22 ± 0.08 vs. 0.31 ± 0.14, p = 0.018 for MLR; 14.9% ± 2.0% vs. 16.1% ± 2.5%, p = 0.027 for RDW). Among carcinoma cases, high-grade tumors demonstrated significantly elevated MLR compared to low-grade tumors (0.33 ± 0.16 vs. 0.25 ± 0.11, p = 0.028). Advanced FIGO stage was strongly associated with higher MLR (0.39 ± 0.14 vs. 0.24 ± 0.09, p = 0.004) and elevated RDW (17.06% ± 2.66% vs. 15.31% ± 2.18%, p = 0.017). Logistic regression confirmed MLR as a powerful independent predictor of malignancy (OR = 2.84, p = 0.011).

Conclusion: Pretreatment MLR and RDW are valuable, cost-effective inflammatory biomarkers that reliably predict higher tumor grade and advanced FIGO stage in endometrial carcinoma, facilitating enhanced preoperative risk stratification.

Keywords: MLR, RDW, FIGO.

INTRODUCTION

Endometrial carcinoma represents one of the most common gynecological malignancies globally, showing rising incidence rates in transitioning economies. The clinical course and choice of therapeutic modalities are dictated by the International Federation of Gynecology and Obstetrics (FIGO) stage and histological tumor grade. Accurate estimation of these factors traditionally relies on invasive and resource-intensive staging surgeries. Consequently, there is a compelling need for simple, universally reproducible, and inexpensive biomarkers that can provide accurate preoperative insight into tumor aggressiveness.[1,2]

Systemic inflammation is intricately linked to the initiation, progression, and metastatic dissemination

of solid malignancies. The tumor microenvironment induces systemic hematological changes, driving alterations in circulating leukocytes and red blood cell characteristics. Among these systemic changes, the monocyte-to-lymphocyte ratio (MLR) reflects a balance between the pro-tumorigenic properties of monocytes (which differentiate into tumor-associated macrophages) and the anti-tumor immune response mediated by lymphocytes.[3,4]

Concurrently, red cell distribution width (RDW), a classic index of erythrocyte size variation, is increasingly recognized as a robust marker of chronic systemic inflammation and oxidative stress. Chronic inflammation impairs iron metabolism and suppresses erythropoiesis, causing an increased release of immature, heterogenous erythrocytes into circulation. Elevated pretreatment RDW has been correlated with poor clinical presentation and advanced disease status in multiple visceral malignancies.[5,6]

While definitive staging remains histopathological, utilizing routine hematological indices like MLR and RDW can provide a continuous biological readout of the tumor-host dynamic. Integrating these accessible parameters into routine clinical practice can optimize early surgical planning, especially in resource-limited environments. This study aims to evaluate the predictive efficacy of pretreatment MLR and RDW concerning tumor grade and clinical FIGO stage in endometrial carcinoma.[7,8]

MATERIALS AND METHODS

Study Design and Setting: This cross-sectional observational study was conducted in the Department of Pathology at Geetanjali Medical College and Hospital, Udaipur, Rajasthan, over an 18-month period. Ethical clearance was formally granted by the Institutional Ethics Committee, and written informed consent was acquired from all participating subjects prior to evaluation.

Patient Selection: A total of 100 consecutive patients presenting with abnormal uterine bleeding (AUB) or postmenopausal bleeding who underwent endometrial biopsy or definitive hysterectomy were enrolled. The cohort was categorized based on final histopathology into benign endometrial disease (n = 47), endometrial hyperplasia without atypia (n = 8), endometrial hyperplasia with atypia (n = 4), and endometrial carcinoma (n = 41).

Inclusion and Exclusion Criteria

All tissue specimens received during the study period accompanied by pre-treatment routine blood records were included. Patients were strictly excluded if they presented with known concurrent autoimmune disorders, systemic myeloproliferative diseases, recent history of acute urinary tract infections, prior splenectomy, or documented use of chronic anti-inflammatory medications that could distort baseline hematological profiles.

Laboratory and Histopathological Evaluation

Pretreatment peripheral blood samples collected in EDTA tubes were processed using an automated hematology analyzer to obtain absolute counts and red cell indices. MLR was calculated as the absolute monocyte count divided by the absolute lymphocyte count, while RDW was recorded directly as a percentage. All tissue specimens were fixed in 10% neutral buffered formalin, routinely processed into paraffin block sections at 4 □m, stained with Hematoxylin and Eosin (H&E), and evaluated according to the WHO classification system and current FIGO staging guidelines.

Statistical Analysis

Statistical processing was executed using SPSS version 15.0 for Windows. Quantitative variables were expressed as mean ± standard deviation (SD), and statistical significance across diagnostic subsets was evaluated using Student's unpaired t-tests or ANOVA where appropriate. Binary logistic regression was performed to compute odds ratios (OR) for predictors of malignancy, and Receiver Operating Characteristic (ROC) curve analysis was utilized to establish diagnostic sensitivity and specificity, taking a p-value < 0.05 as statistically significant.

RESULTS

Demographic and Clinical Baseline Attributes.

Table 1: Progressive changes in MLR and RDW across histopathological categories

Parameter	Benign	Hyperplasia (No Atypia)	Hyperplasia (Atypia)	Carcinoma	p-value
MLR (mean ± SD)	0.22 ± 0.08	0.25 ± 0.09	0.28 ± 0.10	0.31 ± 0.14	0.018
RDW % (mean ± SD)	14.9 ± 2.0	15.2 ± 2.1	15.5 ± 2.3	16.1 ± 2.5	0.027

Table 2: Age distribution of study participants (Both Benign and Malignant) (N=100)

Age group (years)	Number of patients	Percentage (%)
<40	21	21.0
41–50	37	37.0
51–60	19	19.0
61–70	14	14.0
>70	9	9.0
Total	100	100.0

The above table illustrate that out of total study participants, 21 (21.0%) were aged <40 years, 37 (37.0%) were 41–50 years, 19 (19.0%) were 51–60 years, 14 (14.0%) were 61–70 years and 9 (9.0%) were >70 years with mean age 49.28 ± 14.10 years.

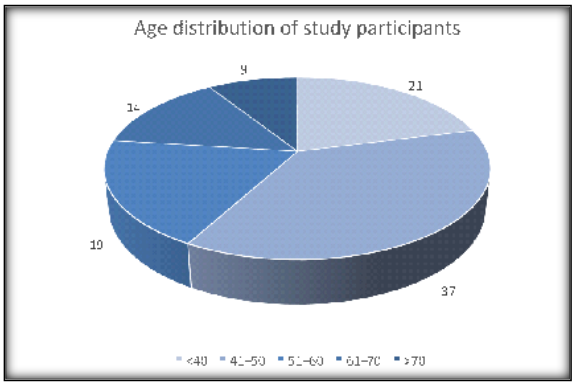

Figure 1: ?

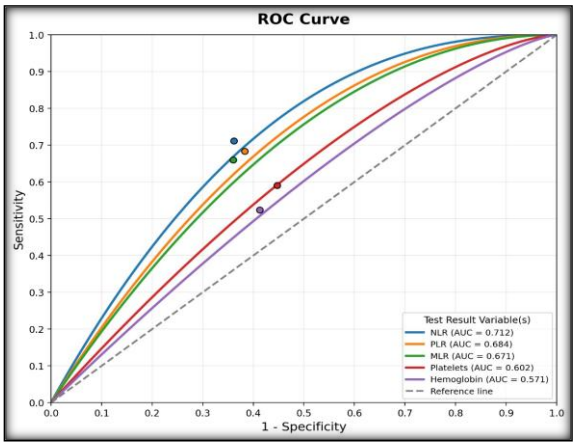

Figure 2:

The mean age of the entire cohort (N = 100) was 49.28 ± 14.10 years, with the highest concentration of patients falling within the 41–50 age range (37.0%). However, a highly significant progressive rise in mean age was observed across the pathological spectrum, moving from 43.8 ± 10.2 years in benign lesions to 47.6 ± 8.7 years in hyperplasia without atypia, 52.8 ± 7.9 years in hyperplasia with atypia, and reaching 58.4 ± 10.6 years in established endometrial carcinoma ($p < 0.001$).

Histopathological Distribution of Carcinoma Cases

Among the 41 patients confirmed with endometrial carcinoma, endometrioid adenocarcinoma was identified as the predominant histological variant, accounting for 34 cases (82.9%). Mixed/other epithelial malignancies were observed in 5 cases (12.2%), while serous carcinoma and clear cell carcinoma were each diagnosed in 1 case (2.4%). Regarding differentiation, low-grade lesions (Grade 1 and 2) made up the substantial majority, with Grade 1 representing 24 cases (58.5%), Grade 2 representing 12 cases (29.3%), and Grade 3 high-grade lesions found in 5 cases (12.2%).

FIGO Staging Characteristics

Staging data available for the surgically managed carcinoma group showed a high prevalence of early-stage disease. Stage IA was identified in 17 cases (63.0%), Stage IB in 3 cases (11.1%), Stage II in 1 case (3.7%), Stage IIIA in 3 cases (11.1%), Stage IIIC1 in 2 cases (7.4%), and Stage IIIC2 in 1 case (3.7%). Cumulatively, early-stage presentation (Stages I and II) encompassed the majority of the staged carcinoma cohort.

Distribution of Pretreatment MLR and RDW across Disease Categories

A clear, statistically significant escalation in both pretreatment MLR and RDW values was observed across the tissue categories. The baseline mean MLR rose from 0.22 ± 0.08 in benign pathologies to 0.25 ± 0.09 in hyperplasia without atypia, 0.28 ± 0.10 in hyperplasia with atypia, and reached a peak of
0.31 ± 0.14 within the carcinoma group ($p = 0.018$). Similarly, RDW percentages expanded gradually from 14.9% ± 2.0% in the benign cohort to 15.2% ± 2.1% in non-atypical hyperplasia, 15.5% ± 2.3% in atypical hyperplasia, and 16.1% ± 2.5% in frank carcinoma ($p = 0.027$).

Correlation of MLR and RDW with Tumor Grade and FIGO Stage

Focusing exclusively on the endometrial carcinoma subset (n = 41), pretreatment MLR values were significantly higher in high-grade (Grade 3) tumors compared to low-grade (Grade 1 and 2) variants (0.33
± 0.16 vs. 0.25 ± 0.11, $p = 0.028$). RDW differences between low and high tumor grades did not meet statistical significance (15.56% ± 2.64% vs. 15.32% ± 2.75%, $p = 0.774$). When evaluated against anatomical disease extent, both markers showed significant correlations with advanced FIGO stages. Patients presenting with advanced-stage disease displayed significantly higher pretreatment MLR levels (0.39 ± 0.14 vs. 0.24 ± 0.09, $p = 0.004$) and markedly elevated RDW levels (17.06% ± 2.66% vs. 15.31%
± 2.18%, $p = 0.017$) relative to patients with early-stage disease.

Diagnostic Predictive Efficacy and Logistic Regression

ROC curve analysis for differentiating carcinoma from non-carcinoma lesions demonstrated an Area Under the Curve (AUC) of 0.671 for MLR, yielding a clinical sensitivity of 66.0% and a specificity of 64.0%. In comparison, conventional single metrics such as isolated hemoglobin (AUC = 0.571) and absolute platelet counts (AUC = 0.602) demonstrated distinctly inferior diagnostic performance. Multivariate logistic regression analysis highlighted that pretreatment inflammatory parameters act as robust independent predictors of carcinoma. MLR emerged as a highly powerful independent predictor among the markers,

demonstrating a notable odds ratio (OR = 2.84, 95% CI, p = 0.011). Age also maintained independent predictive significance (OR = 1.03, p = 0.031), while conventional isolated variables like total hemoglobin and absolute platelets did not function as significant independent factors.

DISCUSSION

The results of the present study confirm that pretreatment hematological inflammatory indices undergo systematic elevations that parallel the biological progression of endometrial disease. The significant increase in MLR and RDW from benign configurations to atypical hyperplastic states and invasive carcinoma highlights an escalating systemic inflammatory reaction. Our analysis confirms that these simple, readily available biomarkers correlate with aggressive clinicopathological features, notably higher histopathological tumor grade and advanced anatomical FIGO stage.[9,10]

Evaluating the monocyte-to-lymphocyte ratio provides an indirect evaluation of the tumor microenvironment. Monocytes migrate into tumor tissue and transform into tumor-associated macrophages (TAMs), which secrete angiogenic factors, degrade extracellular matrix, and promote local invasion.[11,12] Conversely, lymphocytes are essential components of host cell-mediated immunity, acting to suppress tumor cell proliferation and survival. Consequently, an elevated MLR reflects an immune profile shifted toward tumor progression and away from effective host surveillance, explaining its association with advanced FIGO stages and high-grade tumors observed in our study.[13,14]

Simultaneously, RDW is altered by sustained systemic inflammation. Inflammatory cytokines, such as interleukin-6 and tumor necrosis factor-alpha, disrupt iron homeostasis, inhibit erythropoietin production, and shorten the lifespan of circulating red blood cells.[15,16] This results in the premature release of immature erythrocytes into the bloodstream, manifesting as significant anisocytosis. The high RDW values noted in advanced FIGO stages in this study reflect a severe systemic inflammatory state associated with high tumor burden and deeper tissue invasion.[17,18]

Our logistic regression data highlights the independent value of these combined indices, where MLR demonstrated an impressive odds ratio of 2.84 for identifying malignancy. This demonstrates that analyzing ratios of interacting cell lines is superior to evaluating individual absolute leukocyte or platelet counts.[19,20] These findings support using these routine, cost-effective inflammatory parameters for preoperative risk stratification, helping clinicians identify patients who may require comprehensive lymphadenectomy or specialized tertiary oncological care.[21,22]

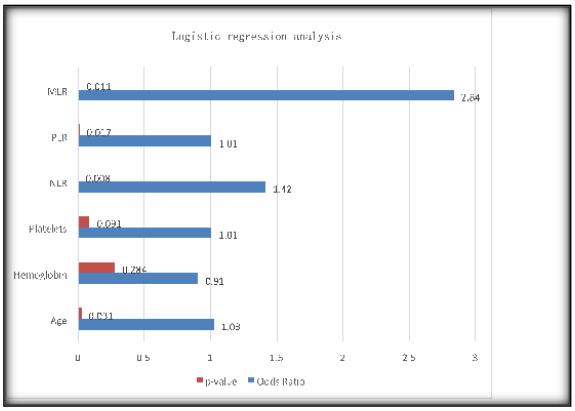

Figure 3

Comparison with Similar Studies

In a related investigation, Marin et al. evaluated the clinical correlations between serological markers and endometrial cancer staging. They observed that inflammatory indices, including MLR, were significantly higher in the malignancy group compared to the hyperplastic group. Their ROC curves and regression models supported the role of these markers in tracking systemic inflammation, concluding that widespread clinical utilization of these cost-effective parameters could enhance diagnostic accuracy in resource-limited institutions.

In another study, Song et al. focused on the prognostic significance of pretreatment leukocyte ratios specifically within non-endometrioid endometrial cancer configurations. They found that an elevated preoperative MLR was a powerful independent predictor of both shortened disease-free survival and poor overall survival. Their survival analysis demonstrated that patients with high baseline MLR had significantly higher recurrence rates, supporting the role of MLR as a cost-effective biomarker for aggressive risk stratification.

Additionally, Zhong et al. examined the relationship between the coefficient of variation of red cell distribution width (RDW-CV) and CA125 in staging endometrial cancer. Their data showed that patients with advanced-stage disease had significantly higher RDW-CV levels alongside reduced baseline hemoglobin values compared to early-stage cohorts. They concluded that elevated RDW reflects a profound systemic inflammatory state and serves as an independent predictor of poor postoperative overall survival.

Furthermore, Cong et al. designed a combined prognostic framework integrating multiple preoperative blood indices, including NLR, PLR, and MLR, in a large cohort of surgically treated endometrial cancer patients. Their findings showed that while individual elevations in MLR predicted poor clinical survival, combining all three inflammatory ratios provided superior prognostic accuracy. This composite approach yielded a high concordance index on survival nomograms, reinforcing the value of blood-derived inflammatory ratios for individualized treatment planning.

Finally, Rafiei Sorouri et al. investigated the diagnostic utility of RDW and mean platelet volume (MPV) in women presenting with abnormal uterine bleeding. Their comparisons revealed significantly higher baseline RDW levels in patients with confirmed endometrial carcinoma compared to those with benign hyperplastic changes or normal controls. They concluded that RDW is an inexpensive, accessible marker that can effectively complement histopathological evaluations to differentiate malignant from benign endometrial pathologies.

CONCLUSION

Pretreatment monocyte-to-lymphocyte ratio (MLR) and red cell distribution width (RDW) are reliable, cost-effective, and readily accessible biomarkers that reflect the systemic inflammatory response in endometrial carcinoma. Significant, progressive elevations in MLR and RDW correlate with the transition from benign lesions to hyperplasia and invasive malignancy. Furthermore, elevated pretreatment MLR serves as an independent predictor of higher tumor grade, while both elevated MLR and RDW are strongly associated with advanced FIGO stages. Integrating these routine hematological indices into preoperative evaluations can enhance risk stratification and guide treatment planning, particularly in resource-limited clinical settings.

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