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Hematologic Biomarkers in Reproductive Cancers: Diagnostic and Prognostic Potential

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Abstract

Reproductive cancers—including cervical, ovarian, endometrial, and hormonally linked breast malignancies—remain leading causes of cancer-related morbidity and mortality in women worldwide. Early diagnosis and accurate prognostication are critical for optimizing treatment and improving survival, yet conventional diagnostic tools are often invasive, costly, or limited in sensitivity. Hematologic biomarkers, derived from routine blood tests, are increasingly recognized as valuable, low-cost indicators that reflect tumor-driven systemic inflammation, immune dysregulation, angiogenesis, and hypoxia. Parameters such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR), red cell distribution width (RDW), and mean platelet volume (MPV) have shown diagnostic and prognostic relevance across reproductive cancers. This review synthesizes current evidence on the utility of hematologic biomarkers in detecting disease, predicting treatment response, and stratifying patient risk. It also highlights the biological mechanisms underpinning their associations with tumor progression, outlines their limitations, and identifies future research priorities. Hematologic biomarkers represent promising adjuncts to precision oncology, particularly in resource-limited settings where affordable and accessible tools are urgently needed.

Keywords: Hematologic biomarkers; Reproductive cancers; Prognosis; Inflammation; Precision oncology

Introduction

Reproductive cancers—including cervical, ovarian, endometrial, and hormonally influenced breast cancers—constitute a significant proportion of the global cancer burden, particularly among women of reproductive and post-reproductive age (1). These malignancies are associated with high morbidity and mortality, with cervical and ovarian cancers ranking among the leading causes of cancer deaths in low- and middle-income countries (1, 2). Late-stage presentation, limited access to diagnostic technologies, and disparities in healthcare infrastructure exacerbate poor outcomes (3), underscoring the urgent need for reliable, accessible, and cost-effective biomarkers to improve early detection and prognostic assessment. Current diagnostic strategies for reproductive cancers rely heavily on histopathological examination, imaging modalities, and molecular profiling. While these methods remain the gold standard, they are often invasive, resource-intensive, and subject to variability in interpretation (4). Moreover, they may fail to capture real-time systemic changes in the tumor microenvironment that influence disease progression and treatment response (5). This diagnostic gap has accelerated interest in peripheral blood-derived biomarkers as complementary tools that can provide continuous, minimally invasive, and affordable insights into tumor biology (6).

Hematologic biomarkers are indices obtained from routine complete blood counts, including neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR), red cell distribution width (RDW), and mean platelet volume (MPV). These parameters are not only widely available and inexpensive but also reflect systemic processes central to carcinogenesis such as inflammation, immune evasion, angiogenesis, and hypoxia (7). Their potential to predict clinical outcomes in diverse malignancies has made them attractive candidates for integration into oncology practice (8). The biological underpinnings of hematologic biomarkers are linked to the bidirectional relationship between tumors and the host immune system. Elevated neutrophils promote tumor progression by releasing pro-inflammatory cytokines and proteolytic enzymes, while reduced lymphocytes indicate compromised immune surveillance (9). Similarly, platelets contribute to tumor growth and metastasis through pro-angiogenic factors, and alterations in red cell indices may signal tumor-induced bone marrow dysfunction or systemic hypoxia (10). Together, these mechanisms provide a strong rationale for exploring hematologic parameters as proxies of tumor behavior and prognosis.

Accumulating evidence demonstrates that hematologic biomarkers have diagnostic and prognostic significance in reproductive cancers. For example, high NLR and PLR have been associated with advanced stage, lymph node involvement, and reduced survival in cervical and ovarian cancers (11, 12). Elevated RDW correlates with aggressive disease in endometrial carcinoma (13), while MPV and LMR have shown predictive value in breast cancer progression and treatment outcomes (14). These findings suggest that hematologic biomarkers may serve as inexpensive yet robust tools to complement established diagnostic and prognostic frameworks. The clinical utility of hematologic biomarkers is particularly relevant in resource-limited regions, where advanced molecular tests and imaging modalities are often inaccessible (15). Because complete blood counts are widely available, even in low-resource healthcare systems, hematologic indices could provide an equitable means of enhancing cancer diagnosis, risk stratification, and monitoring (16). Their use may bridge existing gaps in global oncology care, enabling more timely interventions and tailored therapeutic approaches.

This narrative review synthesizes current evidence on the role of hematologic biomarkers in reproductive cancers, with emphasis on their diagnostic and prognostic potential. It explores the biological mechanisms underpinning their clinical relevance, evaluates evidence across cervical, ovarian, endometrial, and breast cancers, and discusses challenges to their integration into

clinical practice. Finally, it identifies future research directions aimed at standardizing cutoff values, validating findings in diverse populations, and developing multimodal biomarker panels that can advance precision oncology in reproductive health.

Aim

The aim of this review is to critically evaluate the role of hematologic biomarkers in reproductive cancers, with a focus on their diagnostic and prognostic potential.

Methods

This narrative review was conducted with the aim of synthesizing and critically evaluating current evidence on hematologic biomarkers in reproductive cancers. Although narrative in design, we adhered to principles of methodological transparency to enhance reproducibility and rigor.

Literature Search Strategy

A comprehensive literature search was carried out between January and August 2025 across three major electronic databases: **PubMed**, **Scopus**, and **Web of Science**. The search strategy combined Medical Subject Headings (MeSH) and free-text terms related to reproductive cancers and hematologic biomarkers. Key search terms included: *"reproductive cancer," "cervical cancer," "ovarian cancer," "endometrial cancer," "prostate cancer," "testicular cancer," "hematologic biomarkers," "blood-based markers," "NLR," "RDW," "platelet indices,"*

"coagulation markers," and *"inflammatory biomarkers."* Boolean operators ("AND," "OR") were used to refine the search. Reference lists of key articles and relevant review papers were also screened to identify additional sources.

Eligibility Criteria

We included studies that met the following criteria:

1. Investigated hematologic or inflammation-based biomarkers in any reproductive cancer.
2. Reported diagnostic, prognostic, or therapeutic associations.
3. Human studies published in English.
4. Observational studies (cohort, case-control, cross-sectional), clinical trials, and systematic reviews.

Exclusion criteria included: animal studies, case reports, commentaries, studies lacking clearly defined outcomes, and articles not focused on reproductive cancers. Studies before 2000 were excluded to maintain relevance to contemporary diagnostic and therapeutic practices.

Study Selection and Appraisal

Two authors independently screened titles and abstracts, followed by full-text assessments for eligible studies. Disagreements were resolved through discussion and consensus. To strengthen analytical depth, each included study was evaluated for key methodological characteristics such as study design, sample size, statistical adjustments, potential confounders, and reported limitations. Higher-quality evidence, including prospective cohorts and randomized studies when available, was prioritized in shaping conclusions.

Data Extraction and Synthesis

The following data were extracted from each article: study design, population characteristics, sample size, biomarker type, analytical methods, key findings, and clinical implications. Findings were synthesized narratively due to heterogeneity in study designs, biomarkers assessed, and outcome measures. Emphasis was placed on integrating biological mechanisms with clinical observations to construct a comprehensive understanding of the diagnostic and prognostic potential of hematologic biomarkers.

Ethical Considerations

As this review utilized published data only, no ethical approval was required.

Biological Rationale Linking Hematology to Reproductive Cancers

The relationship between hematologic parameters and reproductive cancers is rooted in the dynamic interactions between tumor biology and the host hematopoietic and immune systems. Tumors not only alter systemic hematologic profiles but also exploit hematologic pathways to sustain growth, evade immune destruction, and promote metastasis (17). The following mechanisms highlight the biological rationale underpinning the use of hematologic biomarkers as diagnostic and prognostic tools in reproductive cancers (Table 1).

Table 1:Biological Rationale Linking Hematologic Biomarkers to Reproductive Cancers,

Hematologic Biomarker	Underlying Mechanism	Clinical Relevance in Reproductive Cancers	Example Evidence
Neutrophil-to-Lymphocyte Ratio (NLR)	Reflects systemic inflammation: elevated neutrophils promote tumor progression; lymphopenia indicates reduced immune surveillance	Associated with advanced stage, lymph node metastasis, and poor survival in cervical, ovarian, endometrial, and breast cancers	High NLR predicts poor overall survival in ovarian and cervical cancers (18, 19)
Platelet-to-Lymphocyte Ratio (PLR)	Platelets facilitate angiogenesis and metastasis; lymphocytes reflect immune competence	Linked to aggressive tumor biology, recurrence, and chemo resistance across multiple reproductive cancers	Elevated PLR correlates with poor prognosis in ovarian and endometrial cancers (20, 21)
Lymphocyte-to-Monocyte Ratio (LMR)	Monocytes differentiate into tumor-associated macrophages promoting immunosuppression	Low LMR predicts poor survival and increased metastatic potential	Low LMR associated with reduced disease-free survival in endometrial and breast cancers (22)
Red Cell Distribution Width (RDW)	Reflects anisocytosis from tumor-induced hypoxia, inflammation, and nutritional deficiencies	Elevated RDW correlates with advanced disease stage, treatment resistance, and poor prognosis	High RDW predicts reduced progression-free survival in cervical and ovarian cancers (23)
Mean Platelet Volume (MPV)	Marker of platelet activation; linked to thrombotic risk and tumor metastasis	Higher MPV associated with metastatic potential and tumor aggressiveness	Elevated MPV predicts disease progression in breast and ovarian cancers (24)

1. Inflammation and Neutrophil Dynamics

Chronic inflammation is a recognized hallmark of carcinogenesis, and reproductive cancers frequently evolve in inflammatory microenvironments (25). Neutrophils, key mediators of the innate immune response, are often elevated in cancer patients and contribute to tumor progression by secreting pro-inflammatory cytokines, chemokines, and matrix-degrading enzymes. They also promote angiogenesis through the release of vascular endothelial growth factor (VEGF). Conversely, lymphocyte depletion reflects impaired adaptive immunity and diminished tumor surveillance. The neutrophil-to-lymphocyte ratio (NLR) thus serves as a surrogate marker of the balance between tumor-promoting inflammation and tumor-suppressing immunity (18, 19).

2. Platelets and Tumor Angiogenesis

Platelets play a crucial role in reproductive cancers by facilitating angiogenesis, protecting circulating tumor cells, and enhancing metastatic spread. Activated platelets release growth factors such as VEGF, platelet-derived growth factor (PDGF), and transforming growth factor-beta (TGF-β), which support vascular remodeling and immune evasion. Elevated platelet counts and increased platelet-to-lymphocyte ratio (PLR) are consistently associated with poor outcomes in ovarian, endometrial, and cervical cancers (20, 21) , underscoring the role of platelets as both effectors of tumor progression and accessible prognostic markers.

3. Red Blood Cell Indices and Tumor-Induced Hypoxia

Alterations in red cell indices, particularly red cell distribution width (RDW) and mean corpuscular volume (MCV), often mirror systemic hypoxia, inflammation, or nutritional deficiencies induced by malignancy (23, 26, 27). Elevated RDW has been associated with aggressive disease biology and poor prognosis in ovarian and cervical cancers. Hypoxia-driven erythropoietin responses and bone marrow stress can cause anisocytosis, making RDW a sensitive, albeit indirect, marker of disease burden and tumor-host interactions (23, 28).

4. Monocytes and Immunosuppressive Pathways

Monocytes contribute to tumor progression by differentiating into tumor-associated macrophages (TAMs), which foster immune tolerance, extracellular matrix remodeling, and angiogenesis (29). A reduced lymphocyte-to-monocyte ratio (LMR) has been correlated with adverse outcomes in reproductive cancers, as it reflects a systemic shift toward immunosuppression (22). Elevated monocyte counts are further linked to metastatic potential, providing mechanistic support for LMR as a prognostic biomarker (30-32).

5. Platelet Indices and Tumor Aggressiveness

Beyond platelet counts, platelet indices such as mean platelet volume (MPV) and platelet distribution width (PDW) provide additional insights into tumor biology. Elevated MPV suggests increased platelet activation, which correlates with heightened thrombotic risk and metastatic activity (20, 21,33-35). These indices have been reported as predictors of disease progression in breast and ovarian cancers, highlighting their relevance as dynamic hematologic markers of tumor aggressiveness.

6. Integration of Hematologic Pathways

The convergence of these hematologic mechanisms underscores the multifaceted role of blood-derived indices in reproductive cancers. Tumor-induced inflammation, immune evasion, angiogenesis, and hypoxia collectively shape the hematologic landscape, which can be captured through simple, cost-effective parameters measurable in routine clinical practice (18-23). These biomarkers therefore hold strong biological justification for integration into diagnostic, prognostic, and therapeutic frameworks.

Hematologic Biomarkers in Specific Reproductive Cancers

1. Cervical Cancer

Cervical cancer, primarily driven by persistent high-risk human papillomavirus (HPV) infection, is strongly influenced by inflammation and immune modulation (36, 37). Hematologic biomarkers such as NLR, PLR, and RDW have been studied extensively in this context. Elevated NLR is consistently associated with advanced FIGO stage, lymph node metastasis, and poor overall survival. PLR has similarly been linked with aggressive tumor biology, suggesting a role of platelet-mediated angiogenesis in disease progression. RDW, reflecting systemic inflammation and hypoxia, correlates with treatment resistance and reduced progression-free survival. Pre-treatment biomarker levels may also predict outcomes following radiotherapy and chemoradiation, making them valuable tools in patient stratification (18, 19).

2. Ovarian Cancer

Ovarian cancer often presents at an advanced stage due to its insidious onset and lack of specific symptoms. Hematologic biomarkers have shown significant prognostic potential in this setting. (38). Elevated NLR has been associated with poor response to platinum-based chemotherapy, shorter progression-free survival, and worse overall survival. PLR also predicts recurrence and chemoresistance, emphasizing the contribution of platelet-driven angiogenesis and immune modulation in tumor progression. RDW has emerged as an independent predictor of survival, while dynamic changes in these indices during treatment may provide early indicators of therapeutic efficacy (20, 21). Given the heterogeneity of ovarian cancer, integrating hematologic biomarkers with molecular subtyping could refine patient-specific management

3. Endometrial Cancer

Endometrial cancer, the most common gynecological malignancy in high-income countries, exhibits hematologic alterations that mirror tumor aggressiveness (39). Elevated NLR has been linked to high-grade histological subtypes, deep myometrial invasion, and lymphovascular space involvement. A low LMR correlates with reduced disease-free survival, reflecting immunosuppressive mechanisms mediated by monocytes and macrophage recruitment. PLR has also been identified as an adverse prognostic factor, particularly in predicting recurrence and metastasis (22, 23). These biomarkers may help refine surgical decision-making, such as the need for lymphadenectomy or adjuvant therapy.

4. Breast Cancer

Although breast cancer is not confined to the reproductive tract, its hormonal regulation and systemic hematologic interactions align it closely with reproductive cancers (40). Numerous studies have highlighted the role of hematologic biomarkers in predicting disease course. Elevated NLR is a robust marker of poor prognosis, particularly in triple-negative and HER2-positive subtypes. PLR has been associated with metastatic progression and worse survival outcomes, while MPV correlates with tumor invasiveness and thrombotic complications. RDW has also been linked with advanced stage and reduced overall survival (24, 41) . Importantly, these markers may complement molecular profiling in guiding personalized treatment strategies, including immunotherapy and targeted therapies.

5. Cross-Cancer Perspectives

Across reproductive cancers, hematologic biomarkers share overlapping prognostic patterns, underscoring the central role of inflammation, angiogenesis, and immune dysregulation in tumor biology. While NLR, PLR, and RDW remain the most consistently validated indices, other markers such as LMR and MPV are gaining recognition for their specificity in certain malignancies. Their reproducibility, low cost, and universal availability make them particularly attractive for clinical use. However, their predictive power may

vary by cancer type, stage, and treatment modality, highlighting the need for context-specific interpretation (Table 2).

Table 2: Hematologic Biomarkers in Specific Reproductive Cancers

Cancer Type	Key Hematologic Biomarkers	Prognostic / Diagnostic Value	Clinical Application	Example Evidence
Cervical Cancer	NLR, PLR, RDW	High NLR and PLR predict advanced FIGO stage, lymph node metastasis, and poor overall survival; elevated RDW indicates treatment resistance	Risk stratification, prognosis, monitoring treatment response	(18, 19)
Ovarian Cancer	NLR, PLR, RDW	Elevated NLR and PLR associated with chemoresistance, recurrence, and reduced progression-free survival; RDW predicts overall survival	Prognostic stratification, monitoring therapy response	(20, 21)
Endometrial Cancer	NLR, LMR, PLR	High NLR and low LMR linked to aggressive histological subtypes, lymphovascular invasion, and recurrence; PLR predicts poor prognosis	Preoperative risk assessment, prognosis, guiding adjuvant therapy	(22, 23)
Breast Cancer	NLR, PLR, MPV, RDW	Elevated NLR and PLR predict metastasis and reduced survival, especially in triple-negative and HER2-positive subtypes; MPV and RDW correlate with tumor aggressiveness	Prognostic stratification, treatment monitoring, complementing molecular profiling	(24, 41)

Clinical Applications

Diagnostic Applications

Hematologic biomarkers provide supplementary value in the early detection and differential diagnosis of reproductive cancers. While they cannot replace histopathology or imaging, their accessibility and low cost make them useful adjuncts in screening and triage. Elevated NLR and PLR, for example, may help distinguish malignant from benign adnexal masses in ovarian pathology (42, 43), while RDW has shown promise in differentiating aggressive endometrial tumors from indolent subtypes (13). When combined with conventional diagnostic approaches, hematologic indices can enhance sensitivity and specificity, offering a cost-effective layer of diagnostic support, especially in resource-constrained environments (44).

Prognostic Stratification

The most established role of hematologic biomarkers in reproductive cancers lies in their prognostic capacity (45). Numerous studies have demonstrated strong associations between elevated NLR, PLR, or RDW and adverse clinical outcomes such as advanced stage, lymph node metastasis, recurrence, and reduced overall survival. Conversely, higher LMR has been linked with favorable prognoses (13, 42,46). Incorporating these indices into preoperative and pre-treatment assessments may enable clinicians to stratify patients by risk, tailor therapeutic interventions, and guide the intensity of follow-

up. This approach aligns with the principles of precision oncology, which emphasize individualized risk prediction and management.

Monitoring Treatment Response

Dynamic changes in hematologic biomarkers during therapy may provide valuable information about treatment response and emerging resistance. For instance, a declining NLR during chemotherapy or chemoradiation has been associated with improved response rates and survival in cervical and ovarian cancers (47-50). Similarly, alterations in PLR and MPV during systemic treatment may serve as early indicators of treatment efficacy or impending disease progression (51). The ability to monitor these markers longitudinally through routine blood counts offers a practical advantage over repeated imaging or invasive procedures.

Predicting Therapy-Related Toxicity

Emerging evidence suggests that hematologic biomarkers may also serve as predictors of treatment-related complications. Elevated pre-treatment NLR has been associated with greater risk of radiation-induced toxicity in cervical cancer patients, while high PLR has correlated with increased chemotherapy-related adverse events (52-54). Such predictive value could help oncologists anticipate complications, optimize supportive care, and minimize treatment interruptions, ultimately improving patient outcomes.

Integration into Multimodal Models

The clinical impact of hematologic biomarkers is maximized when they are integrated with established prognostic models, including molecular markers, imaging findings, and clinical variables. Composite scoring systems that combine NLR, PLR, or LMR with tumor markers such as CA-125 or CA-15-3 have shown improved predictive performance in ovarian and breast cancers (55, 56). Similarly, combining hematologic indices with genomic and proteomic data may yield more powerful prognostic models, supporting individualized therapy planning and clinical decision-making (57, 58).

Potential for Resource-Limited Settings

Hematologic biomarkers hold particular promise in resource-limited settings, where access to advanced diagnostic tools such as genomic profiling, high-resolution imaging, and specialized pathology services is often restricted. Because blood-based indices are inexpensive, widely available, and routinely measured in most clinical environments, they offer a practical avenue for improving cancer detection, prognostic assessment, and treatment monitoring in low- and middle-income countries (59).In many parts of sub-Saharan Africa, for example, patients with cervical or ovarian cancer frequently present at advanced stages due to limited screening infrastructure. Incorporating simple biomarkers such as NLR, RDW, and platelet indices into routine evaluation can strengthen triage decisions, allowing clinicians to identify high-risk individuals who need urgent imaging or referral to tertiary cancer centres. In Zimbabwe, Ethiopia, and Malawi, complete blood count (CBC) parameters are among the most consistently available laboratory tests, making them suitable for integration into local clinical pathways (60).

Similar opportunities exist in South and Southeast Asia, where high patient volumes and constrained laboratory capacity often challenge cancer care. Studies from India and Bangladesh have demonstrated that adding hematologic biomarkers to standard clinical evaluation improves the ability to differentiate between benign and malignant pelvic masses when imaging is limited. In rural settings where follow-up delays are common, biomarkers such as platelet-to-lymphocyte ratio or fibrinogen levels may also assist in prioritising patients requiring earlier intervention (61).Latin American health systems, particularly in regions with uneven access to oncology services, have also explored the use of hematologic indices to supplement diagnostic decision-making for breast and gynecologic malignancies. Here, biomarkers serve as a cost-effective bridge in settings where molecular

assays are not consistently available or affordable (62). Hematologic biomarkers offer an adaptable, scalable, and equitable diagnostic support tool across diverse resource-limited environments. By leveraging tests already embedded within routine clinical workflows, health systems can strengthen early detection and personalized care without significant capital investment. As global efforts continue to focus on reducing disparities in cancer outcomes, these biomarkers provide a feasible and impactful strategy for improving reproductive cancer management in under-resourced settings (63).

Specific Advantages of Hematologic Biomarkers

Hematologic biomarkers offer several distinct advantages that make them particularly valuable in the management of reproductive cancers. Unlike many molecular and imaging-based tools, these markers are derived from simple, routinely available blood tests, positioning them as accessible and cost-effective components of clinical care. Their widespread availability across primary, secondary, and tertiary health facilities allows clinicians to extract meaningful biological information without requiring specialized infrastructure or advanced laboratory capacity (61).Cost-effectiveness is a key advantage, especially in settings where healthcare resources are limited. Complete blood counts, coagulation panels, and inflammatory markers are among the least expensive investigations in oncology practice, yet they capture essential insights into tumor-associated inflammation, immune dysregulation, metabolic stress, and coagulation abnormalities. This makes hematologic biomarkers an attractive adjunct for improving risk stratification and treatment planning while minimizing financial burden on patients and healthcare systems (62).

Another strength lies in their utility for longitudinal monitoring. Because blood-based indices can be measured repeatedly with minimal cost and logistical complexity, they enable dynamic assessment of treatment response, early detection of progression, and identification of emerging therapeutic resistance. Trends in NLR, platelet indices, RDW, or fibrinogen levels can provide early warning signals that complement imaging and clinical evaluation, particularly during chemotherapy, hormonal therapy, or immunotherapy (63).Despite their widespread availability, hematologic biomarkers remain underutilized in many low-resource settings. Their potential is substantial: they can be integrated into existing diagnostic pathways without major investment; they support early triage and referral decisions; and they help compensate for gaps in access to imaging or molecular diagnostics. In regions where delayed presentation is common and diagnostic resources are strained, these markers offer a practical pathway to strengthen cancer detection and patient management (64).

Limitations and Research Gaps

Despite growing evidence supporting hematologic biomarkers as useful tools in reproductive cancers, several limitations constrain their widespread clinical adoption. First, there is a lack of standardized cutoff values across studies. Different investigators have used varying thresholds for NLR, PLR, RDW, and other indices, leading to inconsistent results and reduced reproducibility. Without harmonized criteria, comparisons across populations and cancer types remain difficult, limiting their clinical reliability. Second, hematologic biomarkers are non-specific and can be influenced by numerous physiological and pathological conditions unrelated to cancer. Infections, autoimmune diseases, obesity, metabolic disorders, and even psychological stress can alter leukocyte ratios and platelet indices, introducing confounding variables. This lack of specificity challenges their role as standalone markers of malignancy and underscores the need for careful interpretation within the broader clinical context (64).

Third, most available studies are retrospective, single-center, and heterogeneous in design. Many involve relatively small sample sizes, limited follow-up periods, or restricted ethnic and

geographic representation. These methodological weaknesses reduce the generalizability of findings and highlight the need for large, prospective, multicenter trials to validate associations and refine their prognostic significance. Fourth, there is limited integration of hematologic biomarkers with molecular, genomic, and imaging-based tools that currently drive precision oncology. Although composite models incorporating hematologic indices and tumor markers (e.g., CA-125, CA-15-3) show promise, few have been externally validated. Bridging the gap between low-cost hematologic data and high-precision molecular platforms remains an underexplored avenue for advancing cancer prognostication (63). Fifth, dynamic changes in hematologic biomarkers during therapy are not consistently monitored in clinical practice. Longitudinal studies exploring how these indices evolve during chemotherapy, radiotherapy, or immunotherapy are scarce. Understanding temporal shifts could provide deeper insights into treatment response, resistance mechanisms, and disease recurrence, but current evidence is insufficient. Few studies have evaluated the utility of hematologic biomarkers in low- and middle-income countries, where they may offer the greatest benefit due to limited access to advanced diagnostics. Generating context-specific data from these settings is critical to ensuring global applicability and equity in cancer care (64).

Integration of Hematologic Biomarkers into Multimodal Clinical Models

The growing interest in precision oncology has highlighted the value of combining diverse data sources to improve diagnostic accuracy, prognostic precision, and therapeutic decision-making. Hematologic biomarkers, given their accessibility and strong biological relevance, can complement existing clinical, radiologic, and molecular tools within multimodal predictive frameworks (60).Hematologic indices such as NLR, platelet-based markers, RDW, and fibrinogen reflect real-time systemic inflammation, angiogenesis, and immune dysregulation. When integrated into multimodal models alongside imaging features, genomic signatures, and clinical staging, these biomarkers enhance the sensitivity and specificity of risk stratification algorithms. For example, adding NLR or platelet indices to radiologic scoring systems in ovarian or endometrial cancer may help refine preoperative assessments of tumor aggressiveness or lymph node involvement. Similarly, in prostate cancer, hematologic markers combined with PSA dynamics and MRI findings contribute to more nuanced predictions of disease progression (61-62).

Machine learning and artificial intelligence approaches have further advanced the potential for such integration. These models can combine high-dimensional clinical variables with simple hematologic markers to predict recurrence, chemoresistance, or survival with greater accuracy than conventional methods alone. Incorporating dynamic changes in biomarkers during treatment provides an additional layer of adaptability, offering early warning signals of suboptimal response or impending relapse (63).The incorporation of hematologic biomarkers into multimodal clinical models serves not only to improve precision but also to bridge diagnostic equity across diverse health systems. Their low cost and universal availability position them as practical components in integrated predictive tools that can be applied in both high-income and resource-limited settings. As multimodal oncology strategies continue to evolve, hematologic biomarkers offer a biologically grounded and operationally feasible layer within comprehensive clinical decision frameworks (64).

Conclusion

Hematologic biomarkers represent an emerging and clinically relevant frontier in the management of reproductive cancers. Derived from routine blood counts, indices such as NLR, PLR, LMR, RDW, and MPV provide valuable insights into systemic inflammation, immune balance, angiogenesis, and hypoxia—hallmarks of tumor progression. Evidence across cervical, ovarian, endometrial, and breast cancers demonstrates their diagnostic utility, prognostic power, and potential role in treatment monitoring. The

advantages of hematologic biomarkers lie in their accessibility, affordability, and reproducibility, making them particularly attractive for use in both advanced healthcare systems and resource-limited settings. Their incorporation into risk stratification models could refine patient selection for aggressive therapies, guide surveillance strategies, and complement molecular and imaging-based diagnostics. However, challenges remain, including the lack of standardized cutoff values, susceptibility to confounding conditions, and limited validation in large, prospective, and ethnically diverse cohorts. Addressing these gaps through robust multicenter studies and integrating hematologic indices with genomic, proteomic, and imaging biomarkers will be key to unlocking their full clinical potential.

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