OPEN ACCESS

Scholars International Journal of Obstetrics and Gynecology

Abbreviated Key Title: Sch Int J Obstet Gynec
ISSN 2616-8235 (Print) |ISSN 2617-3492 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Original Research Article

Distribution Width (RDW) between Benign Endometrial Disease and Malignant Endometrial Disease

Dr. Jannatul Islam[1*], Prof. Dr. Jannatul Ferdous[2], Dr. Farhana Khatoon[3], Dr. Mehriban Amatullah[4], Dr. Fatema Nihar[5], Dr. Naznine Akter[6], Dr. Syfun Naher[7], Dr. Moushume Akther Liza[8], Dr. Sunzia Sayed[9], Dr. Lubna Yasmin[10], Dr. Jahangir Alam[11]

[1]Medical Officer, Department of Obstetrics and Gynecology, Upazila Health Complex, Daudcandi, Cumilla, Bangladesh
[2]Professor, Department of Gynecological Oncology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, Bangladesh
[3]Associate Professor, Department of Gynecological Oncology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, Bangladesh
[4]Assistant Professor, Department of Obstetrics and Gynecology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, Bangladesh
[5]Assistant Register, Department of Gynecological Oncology, National Institute of Cancer and Research Hospital (NICRH), Dhaka, Bangladesh
[6]Assistant Professor, Department of Obstetrics and Gynecology, Institute of Health Technology, Dhaka, Bangladesh
[7]Upazila Health & Family Planning Officer, Zanjira Upazila Health Complex, Shariatpur, Bangladesh
[8]Resident, Department of Gynaecological Oncology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh
[9]Resident, Department of Gynaecological Oncology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh
[10]Medical Officer, OSD, Directorate General of Health Services (DGHS), Dhaka, Bangladesh
[11]Child Specialist, Department of Pediatrics, Jaber Al-Ahmed Armed Forces Hospital, Kuwait

DOI: https://doi.org/10.36348/sijog.2024.v07i12.011 | **Received:** 14.11.2024 | **Accepted:** 21.12.2024 | **Published:** 27.12.2024

***Corresponding author:** Dr. Jannatul Islam
Medical Officer, Department of Obstetrics and Gynecology, Upazila Health Complex, Daudcandi, Cumilla, Bangladesh

Abstract

***Background*:** Red cell distribution width (RDW), a measure of erythrocyte size variation, has been implicated as a potential biomarker in various malignancies. However, its role in distinguishing between benign and malignant endometrial diseases remains unclear. This study aimed to evaluate the diagnostic utility of RDW and its correlation with disease severity in endometrial carcinoma. ***Methods*:** This cross-sectional study included 183 women diagnosed with either benign or malignant endometrial diseases. RDW levels were measured and analyzed for their diagnostic significance. Statistical analysis included independent t-tests to compare RDW values between groups and ROC analysis to determine diagnostic accuracy. Correlation between RDW and FIGO staging was also evaluated. ***Results*:** RDW was significantly higher in the malignant group (46.64±6.18) compared to the benign group (43.05±7.03; $p < 0.001$). A non-significant positive correlation was observed between RDW and FIGO staging ($r = 0.031$, $p = 0.815$). The ROC analysis yielded an area under the curve (AUC) of 0.463 (95% CI: 0.374–0.552; $p = 0.414$). The best cutoff value for RDW was 49.50, with a sensitivity of 17% and specificity of 90%. ***Conclusion*:** While elevated RDW is associated with endometrial malignancy, its diagnostic accuracy is limited. However, RDW may serve as a supplementary marker when combined with other diagnostic tools, particularly in low-resource settings. Further studies with larger cohorts are needed to validate these findings and explore RDW's prognostic value.

Keywords: Red cell distribution width, endometrial carcinoma, benign endometrial disease, diagnostic biomarker, FIGO staging.

INTRODUCTION

Endometrial cancer is one of the most common gynecological malignancies globally, ranking as the sixth most prevalent cancer in women [1]. It primarily affects postmenopausal women, although younger individuals can also be diagnosed, especially those with a history of obesity, hormonal imbalances or familial cancer syndromes such as Lynch syndrome [2, 3]. In

contrast, benign endometrial diseases, including endometrial hyperplasia and polyps, are common non-malignant conditions associated with abnormal uterine bleeding, pelvic pain and infertility [4]. Distinguishing between malignant and benign endometrial conditions is critical for appropriate clinical management, as delayed or misdiagnosed malignancies can significantly affect prognosis and survival outcomes [5].

Despite advancements in imaging and histopathological techniques, the diagnosis of endometrial carcinoma often requires invasive procedures such as fractional curettage or hysteroscopy-guided biopsy [6]. These methods, while effective, are resource-intensive and not universally accessible in low-resource settings [7]. This has fueled the ongoing search for non-invasive, cost-effective diagnostic markers that could support clinicians in distinguishing benign from malignant endometrial conditions [8].

In recent years hematological markers derived from routine complete blood counts (CBCs) have garnered attention in oncology due to their association with systemic inflammation and tumor biology [3]. Among these markers, red blood cell distribution width (RDW) has emerged as a potential diagnostic and prognostic biomarker in various malignancies, including colorectal, gastric and breast cancers [9, 10]. RDW reflects the heterogeneity in the size of circulating red blood cells and is routinely reported as part of standard hematological investigations [11]. Elevated RDW levels are thought to be linked to chronic inflammation, oxidative stress and dysregulated erythropoiesis, all of which are characteristic features of the tumor microenvironment [12].

Studies investigating the role of RDW in endometrial carcinoma are limited, but preliminary findings suggest its potential as a marker to differentiate malignant from benign endometrial conditions [13]. For instance, increased RDW levels have been associated with higher FIGO stages of endometrial cancer, indicating a possible correlation with disease severity [14]. However, conflicting results have also been reported, necessitating further research to validate its diagnostic value [15].

In this context, our study aimed to evaluate the role of RDW in distinguishing between benign and malignant endometrial diseases. By analyzing RDW levels in a cohort of patients with histopathologically confirmed endometrial carcinoma and benign endometrial diseases, we seek to determine its diagnostic accuracy and establish a clinically meaningful cutoff value. Additionally, the study explores the correlation between RDW and clinicopathological characteristics, including FIGO stage, duration of symptoms and family history of malignancy.

Understanding the utility of RDW as a non-invasive, easily accessible marker for endometrial carcinoma could have significant clinical implications, particularly in resource-constrained settings where access to advanced diagnostic tools is limited [11]. If proven effective, RDW could serve as a preliminary screening tool, guiding clinicians in triaging patients for further diagnostic evaluation and enabling timely interventions for those at high risk of malignancy [16].

METHODOLOGY & MATERIALS

This cross-sectional analytic study was conducted in the Department of Gynecological Oncology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, from July 2022 to July 2023. A total of 183 women with abnormal uterine bleeding were included, comprising 61 cases of histopathologically confirmed endometrial carcinoma (FIGO stage I–IV) and 122 cases of benign endometrial disease. Participants were categorized into two groups: Group 1 (cases) and Group 2 (controls).

A purposive sampling technique was used. The sample size was calculated based on previously reported mean RDW values for benign and malignant cases. To enhance accuracy and availability, the study recruited 61 cases and 122 controls, totaling 183 participants.

Inclusion criteria for Group 1 included histopathologically confirmed endometrial carcinoma, while Group 2 included benign endometrial conditions. Patients with other primary cancers, hematological or inflammatory diseases, prior chemotherapy or radiotherapy, local/systemic infections, or serious comorbidities were excluded.

After obtaining IRB approval and informed written consent, 2 ml of venous blood was collected from participants 24–72 hours before laparotomy. Hematological parameters, including RDW, were measured using a fully automated hematology analyzer (XN-2000). Histopathological confirmation of diagnoses was performed via fractional curettage or post-operative specimen analysis. Personal, clinical, and family history data were recorded.

Data were compiled, cleaned, and analyzed using SPSS version 22. Descriptive statistics (means, medians, frequencies) and inferential statistics (independent t-tests, chi-squared tests, and Fisher's exact tests) were applied. ROC curve analysis was performed using MedCalc software to determine the diagnostic performance of RDW, with sensitivity, specificity, and cutoff values calculated using the Youden index. Statistical significance was set at $P < 0.05$.

The study followed the Declaration of Helsinki guidelines, ensuring confidentiality and voluntary participation. Unique IDs were assigned for anonymity, and data were securely stored.

RESULTS

Table I: Age Distribution of the participants (n=183)

Variables	Cases (61)	Control (122)	P value
Age			
24-43	7 (11.5%)	59 (48.4%)	[b]**0.001**[s]
44-63	40 (65.6%)	63 (51.6%)	
≥64	15 (23%)	0	
Mean±SD	55.62±10.24	43.75±6.63	[c]**0.001**[s]
Mean±SD	47.70±9.76		
Median (min-max)	46 (24-72)		

Data presented as n (%), mean±SD, median (min-max)
b= Fisher's Exact test
c= independent t-test
s= significant

Table I presents the age distribution of participants, comparing cases (endometrial carcinoma) and controls (benign endometrial disease). The mean age of the cases was 55.62±10.24 years, significantly higher than the controls at 43.75±6.63 years (p<0.001). The majority of cases (65.6%) were in the 44-63 age group, while most controls (48.4%) were in the 24-43 age group. No control participants were aged ≥64, while 23% of the cases were in this age bracket.

Table II: Distribution of the participants according to malignancy history

Variables	Cases (61)	Control (122)	P value
Family member suffering from endometrial cancer			
Yes	4 (100%)	0	[a]**0.004**[s]
No	57 (31.8%)	122 (68.2%)	
Duration of symptoms (months)			
mean±SD	6.31±2.16	23.25±8.02	[c]**0.001**[s]
mean±SD	17.61±10.41		
Median (min-max)	18 (2-48)		

Data presented as n (%), mean±SD, median (min-max)
a= chi square test
c= independent sample t-test
s= significant

Table II shows the distribution of participants based on family history of endometrial cancer and duration of symptoms. A significant association was observed between malignancy and a family history of endometrial cancer (P = 0.004). The duration of symptoms was notably shorter in malignant cases (mean: 6.31 ± 2.16 months) compared to benign cases (mean: 23.25 ± 8.02 months), with a highly significant difference (P < 0.001).

Table III: Distribution of the participants according to RDW

RDW	Cases (61)	Control (122)	P value
Mean±SD	46.64±6.18	43.05±7.03	[c]**0.001**[s]
Mean±SD	44.26±6.95		
Median (min-max)	44 (2-62)		

Data presented as n (%), mean±SD, median (min-max)
a= chi square test
c= independent sample t-test
s= significant

Table III highlights the distribution of red cell distribution width (RDW) between malignant (cases) and benign (controls) endometrial diseases. The mean RDW was significantly higher in the malignant group (46.64 ± 6.18) compared to the benign group (43.05 ± 7.03, P < 0.001). The median RDW for malignant cases was 44 (range: 2–62), indicating a notable difference in RDW values between the two groups.

Table IV: Correlation of the MPV, PDW and RDW with clinico pathological characteristics

Variables	RDW	P value
	Correlation coefficient	
FIGO stage	0.031	[d]0.815[ns]

d= Spearman's correlation
ns= non-significant at > 0.05 level

Table IV presents the correlation between red cell distribution width (RDW) and FIGO stage of endometrial cancer. The Spearman's correlation coefficient for RDW and FIGO stage was 0.031, indicating no significant correlation (P = 0.815, non-significant at > 0.05 level).

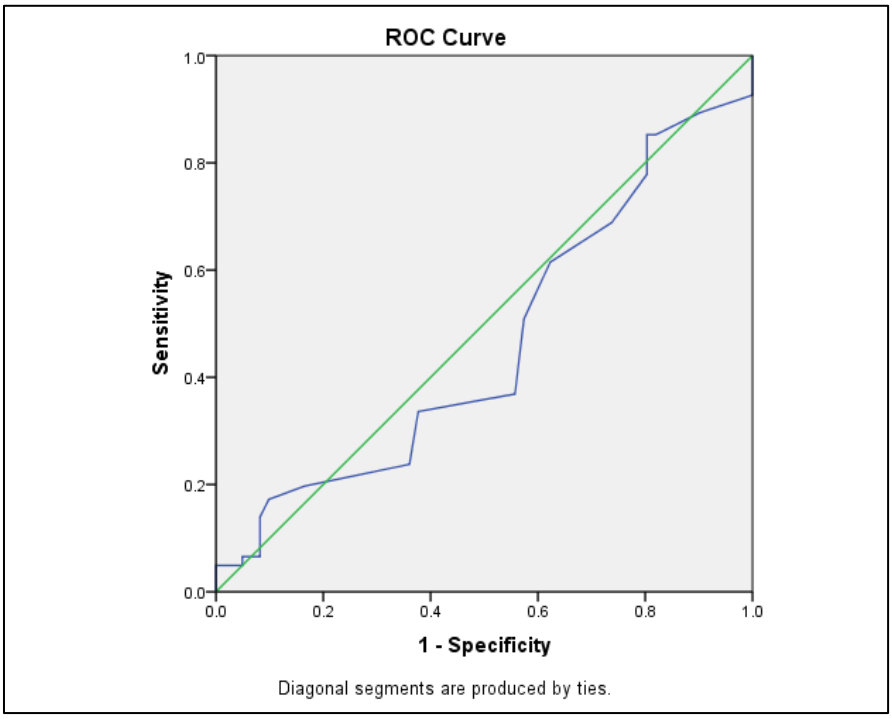

Figure 1: ROC for RDW

Figure 1 shows the ROC curve for RDW in predicting endometrial carcinoma. ROC analysis of RDW to predict endometrial carcinoma found an AUC value of 0.463 (95% CI 0.374-0.552) which was statistically non-significant (P =0.414).

Table V: Determination of cut off value with Youden index

Cutoff value	Sensitivity	Specificity	PPV	NPV	Accuracy	Youden index (j=sen+spe-1)
50.50	0.139	0.918				0.057
49.50	0.172	0.902	0.389	0.725	0.233	0.074
38.50	0.852	0.180				0.033

Table V summarizes the determination of RDW cutoff values using the Youden index. A cut-off value of 49.50 showed the highest Youden index (0.074) with sensitivity 17%, specificity 90%, PPV 39%, NPV 73% and accuracy of 23%.

Table VI: Distribution of the participants according to derived cut-off value

RDW	Cases (61)	Control (122)	P value
<49.50	49 (80.3%)	107 (87.8%)	[a]0.185[ns]
≥49.50	12 (19.7%)	15 (12.3%)	

a= chi-square test
ns= statistically non-significant

Table VI presents the distribution of participants based on the derived RDW cutoff value (49.50). Among cases, 19.7% had RDW ≥49.50 compared to 12.3% of controls. However, this difference

was not statistically significant (P = 0.185, non-significant).

DISCUSSION

Our study analyzed the role of RDW in distinguishing between benign and malignant endometrial diseases. RDW values were significantly higher in the case group (46.64±6.18) compared to the control group (43.05±7.03), with a p-value of <0.001, indicating a strong association between elevated RDW and malignancy. This aligns with findings by Leng *et al*., and Kemal *et al*., who also reported higher RDW levels in endometrial carcinoma cases [17, 18]. Elevated RDW levels are thought to result from chronic inflammation and tumor-associated dysregulation of erythropoiesis, both of which are hallmarks of malignancy. However, conflicting results have been reported in studies such as Oge *et al*., and Yayla Abide *et al*., which found lower RDW levels in cancer patients [19, 20]. These discrepancies may be attributed to differences in study populations, methodologies, and confounding factors like anemia or nutritional deficiencies, which can also influence RDW values.

In our study, RDW demonstrated a non-significant positive correlation with FIGO staging (r = 0.031, p = 0.815). Although the correlation was not statistically significant, the trend suggests that RDW may increase with disease severity. This observation is consistent with findings by Kemal *et al*., who reported a positive correlation between RDW and FIGO stages, highlighting the potential role of RDW as a marker of disease progression [21]. However, the weak correlation observed in our study underscores the need for further research to establish the utility of RDW in staging and prognostication.

The ROC analysis of RDW revealed an AUC value of 0.463 (95% CI: 0.374–0.552), which was not statistically significant (p = 0.414). Despite this, a cutoff value of 49.50 was determined using the Youden index, providing the best balance of sensitivity (17%) and specificity (90%). These findings suggest that while RDW has limited sensitivity as a diagnostic marker, its high specificity makes it useful in ruling out malignancy when levels are below the threshold [22]. This result is clinically relevant, particularly in settings where advanced diagnostic tools are unavailable. For example, a low RDW in patients presenting with abnormal uterine bleeding could help reassure clinicians about the lower likelihood of malignancy, potentially reducing the need for invasive procedures [23].

While RDW alone is not a robust independent predictor of endometrial carcinoma, it holds promise as a supplementary parameter when used in conjunction with other diagnostic tools. Several studies, including Firat *et al*., and Leng *et al*., have highlighted the value of integrating hematological markers such as RDW, neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR) with traditional tumor markers [8, 17]. Such combined models may enhance diagnostic accuracy and provide a more comprehensive assessment of disease status.

RDW's association with malignancy extends beyond gynecological cancers. Elevated RDW has been reported in colorectal, gastric, and lung cancers, where it has been linked to poor prognosis and advanced disease stages. The underlying mechanism involves systemic inflammation, which disrupts erythropoiesis and increases anisocytosis [24]. Inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) play a central role in this process [5]. Our study adds to the growing body of evidence supporting the role of RDW as a marker of cancer-related inflammation.

One of the unique contributions of our study is the potential application of RDW as a low-cost, accessible biomarker in low-resource settings. Advanced diagnostic tools such as MRI, CT scans, or histopathology may not be readily available in many regions [25]. In such contexts, simple hematological parameters like RDW could provide valuable preliminary information to guide clinical decision-making [26]. For instance, patients with elevated RDW values might be prioritized for further investigations, while those with low RDW could be managed conservatively, reducing the burden on healthcare systems [27].

Limitations of the study

The findings of our study must be interpreted in light of certain limitations. The retrospective design and relatively small sample size may limit the generalizability of our results. Additionally, RDW is influenced by various factors, including anemia, nutritional deficiencies, and chronic diseases, which were not fully controlled in our analysis. Future studies should address these confounding variables and explore the dynamics of RDW over time, rather than relying on a single measurement.

CONCLUSION

In conclusion, our study highlights the potential of RDW as a supplementary marker in the differentiation of benign and malignant endometrial diseases. While its diagnostic accuracy as a standalone parameter is limited, its high specificity and association with malignancy make it a valuable adjunct tool, particularly in low-resource settings. By providing a specific RDW cutoff value, we contribute to the growing body of evidence on the clinical utility of hematological markers in gynecological oncology. Further research is needed to validate these findings and explore novel applications of RDW in cancer diagnosis, staging, and prognostication.

Financial support and sponsorship: No funding sources.

Conflicts of interest: There are no conflicts of interest.

Ethical approval: The Institutional Ethics Committee approved the study.

REFERENCES

1. Benagiano, G., Brosens, I., & Lippi, D. (2014). The history of endometriosis. *Gynecologic and obstetric investigation*, *78*(1), 1-9.
2. Sica, A., Allavena, P., & Mantovani, A. (2008). Cancer related inflammation: the macrophage connection. *Cancer letters*, *267*(2), 204-215.
3. Cakal, B., Akoz, A. G., Ustundag, Y., Yalinkilic, M., Ulker, A., & Ankarali, H. (2009). Red cell distribution width for assessment of activity of inflammatory bowel disease. *Digestive diseases and sciences*, *54*, 842-847.
4. Qin, Y., Wang, P., Huang, Z., Huang, G., Tang, J., Guo, Y., ... & Lin, F. (2017). The value of red cell distribution width in patients with ovarian cancer. *Medicine*, *96*(17), e6752.
5. de Gonzalo-Calvo, D., de Luxán-Delgado, B., Rodríguez-González, S., García-Macia, M., Suárez, F. M., Solano, J. J., ... & Coto-Montes, A. (2012). Interleukin 6, soluble tumor necrosis factor receptor I and red blood cell distribution width as biological markers of functional dependence in an elderly population: a translational approach. *Cytokine*, *58*(2), 193-198.
6. Candido, J., & Hagemann, T. (2013). Cancer-related inflammation. *Journal of clinical immunology*, *33*, 79-84.
7. Förhécz, Z., Gombos, T., Borgulya, G., Pozsonyi, Z., Prohászka, Z., & Jánoskuti, L. (2009). Red cell distribution width in heart failure: prediction of clinical events and relationship with markers of ineffective erythropoiesis, inflammation, renal function, and nutritional state. *American heart journal*, *158*(4), 659-666.
8. Firat, A., Ercan, A., Mordeniz, C., & Verit Atmaca, F. F. (2023). Predictive value of hemogram parameters in malignant transformation of the endometrium in patients with different risk factors. *Plos one*, *18*(1), e0279224.
9. Lippi, G., & Plebani, M. (2014). Red blood cell distribution width (RDW) and human pathology. One size fits all. *Clinical Chemistry and Laboratory Medicine (CCLM)*, *52*(9), 1247-1249.
10. Clarke, K., Sagunarthy, R., & Kansal, S. (2008). RDW as an additional marker in inflammatory bowel disease/undifferentiated colitis. *Digestive diseases and sciences*, *53*, 2521-2523.
11. Drayer, S. M., & Catherino, W. H. (2015). Prevalence, morbidity, and current medical management of uterine leiomyomas. *International Journal of Gynecology & Obstetrics*, *131*(2), 117-122.
12. Gao, J., Yang, G., Wen, W., Cai, Q. Y., Zheng, W., Shu, X. O., & Xiang, Y. B. (2016). Impact of known risk factors on endometrial cancer burden in Chinese women. *European Journal of Cancer Prevention*, *25*(4), 329-334.
13. Rhodes, C. J., Howard, L. S., Busbridge, M., Ashby, D., Kondili, E., Gibbs, J. S. R., ... & Wilkins, M. R. (2011). Iron deficiency and raised hepcidin in idiopathic pulmonary arterial hypertension: clinical prevalence, outcomes, and mechanistic insights. *Journal of the American College of Cardiology*, *58*(3), 300-309.
14. McMillan, D. C. (2009). Systemic inflammation, nutritional status and survival in patients with cancer. *Current Opinion in Clinical Nutrition & Metabolic Care*, *12*(3), 223-226.
15. Iwasaki, A., Hamanaka, W., Harnada, T., Maekawa, S., Enatsu, S., & Shirakusa, T. (2007). Significance of platelet counts in patients who underwent surgical treatment for lung metastasis. *International surgery*, *92*(2), 103-109.
16. Günay, E., Sarınç Ulaşlı, S., Akar, O., Ahsen, A., Günay, S., Koyuncu, T., & Ünlü, M. (2014). Neutrophil-to-lymphocyte ratio in chronic obstructive pulmonary disease: a retrospective study. *Inflammation*, *37*, 374-380.
17. Leng, J., Wu, F., & Zhang, L. (2022). Prognostic Significance of Pretreatment Neutrophil-to-Lymphocyte Ratio, Platelet− to− Lymphocyte Ratio, or Monocyte-to-Lymphocyte Ratio in Endometrial Neoplasms: A Systematic Review and Meta− analysis. *Frontiers in Oncology*, *12*, 734948.
18. Kemal, Y., Yucel, I., Ekiz, K., Demirag, G., Yilmaz, B., Teker, F., & Ozdemir, M. (2014). Elevated serum neutrophil to lymphocyte and platelet to lymphocyte ratios could be useful in lung cancer diagnosis. *Asian Pacific journal of cancer prevention*, *15*(6), 2651-2654.
19. Oge, T., T. Yalcin, O., Ozalp, S. S., & Isikci, T. (2013). Platelet volume as a parameter for platelet activation in patients with endometrial cancer. *Journal of Obstetrics and Gynaecology*, *33*(3), 301-304.
20. Yayla Abide, C., Bostanci Ergen, E., Cogendez, E., Kilicci, C., Uzun, F., Ozkaya, E., & Karateke, A. (2018). Evaluation of complete blood count parameters to predict endometrial cancer. *Journal of clinical laboratory analysis*, *32*(6), e22438.
21. Kemal, Y., Demirag, G., Baş, B., Önem, S., Teker, F., & Yücel, İ. (2015). The value of red blood cell distribution width in endometrial cancer. *Clinical Chemistry and Laboratory Medicine (CCLM)*, *53*(5), 823-827.
22. Petric, A. N., Živadinović, R., Mitić, D., Stanojević, M., Živadinović, A., & Kostić, I. (2023). Hematological and biochemical markers in determining the diagnosis and stage prediction of endometrial cancer. *Ginekologia polska*, *94*(4), 283-290.

23. Eoh, K. J., Lee, T. K., Nam, E. J., Kim, S. W., & Kim, Y. T. (2023). Clinical relevance of red blood cell distribution width (rdw) in endometrial cancer: A retrospective single-center experience from Korea. *Cancers*, *15*(15), 3984.
24. Zhang, H., Liang, K., Ke, L., & Tang, S. (2020). Clinical application of red cell distribution width, mean platelet volume, and cancer antigen 125 detection in endometrial cancer. *Journal of Clinical Laboratory Analysis*, *34*(8), e23309.
25. Amant, F., Moerman, P., Neven, P., Timmerman, D., Van Limbergen, E., & Vergote, I. (2005). Endometrial cancer. *The Lancet*, *366*(9484), 491-505.
26. Burke, W. M., Orr, J., Leitao, M., Salom, E., Gehrig, P., Olawaiye, A. B., ... & Society of Gynecologic Oncology Clinical Practice Committee. (2014). Endometrial cancer: a review and current management strategies: part II. *Gynecologic oncology*, *134*(2), 393-402.
27. Suzuki, K., Aiura, K., Kitagou, M., Hoshimoto, S., Takahashi, S., Ueda, M., & Kitajima, M. (2004). Platelets counts closely correlate with the disease-free survival interval of pancreatic cancer patients. *Hepato-gastroenterology*, *51*(57), 847-853.