IJPSR (2024), Volume 15, Issue 9 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 20 March 2024; received in revised form, 17 April 2024; accepted, 13 May 2024; published 01 September 2024

RED CELL DISTRIBUTION WIDTH ASSESSMENT AND HEMATOLOGICAL CORRELATION IN OVARIAN CANCER

Geetha Bhaktha [1], Adhyatma Shetty [2] and S. Veena [* 3]

Department of Biochemistry [1], Siddaganga Medical College and Research Institute, Tumakuru - 572102, Karnataka, India.
Department of Obstetrics & Gynaecology [2], Shimoga Institute of Medical Sciences, Shivamogga - 577201, Karnataka, India.
Department of Pathology [3], Shimoga Institute of Medical Sciences, Shivamogga - 577201, Karnataka, India.

Keywords:

Benign, Malignant, Normal, RDW

Correspondence to Author:
Dr. S. Veena

Assistant Professor,
Department of Pathology, Shivamoga Institute of Medical Sciences,
Shivamogga - 577201, Karnataka, India.

E-mail: drveenas82@gmail.com

ABSTRACT: Ovarian cancer, a major concern in India, is among the leading causes of cancer-related deaths in women. Early detection is crucial due to frequent late-stage diagnoses. Red Cell Distribution Width (RDW), a marker for red blood cell size variability, is promising but lacks extensive study in ovarian cancer. This research aims to correlate RDW with hematological parameters in ovarian cancer patients, potentially improving early detection and prognosis. This study examined data from ovarian cancer patients at Mc Gann's Teaching District Hospital in Shivamogga. Hematological parameters, RDW, were obtained from records, with imaging and histopathological analysis confirming diagnoses. Inclusion criteria Involved ovarian malignancies or benign tumors, while exclusions involved comorbidities or recent treatments impacting blood parameters. Significant differences were observed in RDW ($p = 0.033$), Platelet-to-Lymphocyte Ratio (PLR) ($p = 0.004$), Neutrophil-to-Lymphocyte Ratio (NLR) ($p = 0.001$), Lymphocyte count (L) ($p = 0.0006$), and Neutrophil count (N) ($p = 0.003$) among the case, control, and normal groups. Post hoc analysis revealed significant disparities between the case and control groups for PLR ($p = 0.003$), NLR ($p = 0.002$), L ($p = 0.001$), and N ($p = 0.005$) parameters. Notably, RDW showed a significant difference primarily between the groups. The results imply an association between RDW and ovarian cancer, suggesting its potential as a diagnostic and prognostic biomarker. Further research is needed to understand the clinical significance and explore RDW's role in ovarian cancer management. Early detection through RDW assessment may enhance patient outcomes and reduce mortality rates.

INTRODUCTION: Ovarian cancer holds the rank of the third most prevalent cancer among women in India and eighth globally [1]. Unfortunately, it's also a leading contributor to cancer-related mortality among Indian women [1].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.15(9).2722-26

This article can be accessed online on www.ijpsr.com

DOI link: https://doi.org/10.13040/IJPSR.0975-8232.15(9).2722-26

A striking discrepancy emerges when considering the 5 year survival rates, with a promising 94% survival for Stage I diagnoses and a dismal 28% for the majority of cases diagnosed at Stages III and IV [2].

Notably, the incidence of ovarian cancer displays an age-dependent increase, notably peaking between ages 55-64, with recorded age-adjusted incidence rates ranging from 0.9 to 8.4 per 100,000 women across different Indian population-based cancer registries [3]. Alarming is the fact that the majority of cases are detected at advanced stages.

Given the low population prevalence, screening specificity becomes crucial to maintain an acceptable positive predictive value, particularly as screen-positive cases often necessitate invasive follow-up tests. In contrast, several Western countries have witnessed declining trends in ovarian cancer incidence and mortality, possibly attributable to factors such as increased oral contraceptive use, reduced post-menopausal hormone replacement therapy, and the adoption of risk-reduction surgeries [2]. The discovery of cost-effective biological markers that enhance early ovarian cancer diagnosis and prognosis assessment holds significant clinical importance. The red cell distribution width (RDW) is a parameter indicating the variability in the size of red blood cells and is routinely used in clinical assessments of anemia-related conditions [4]. Recent research, however, has unveiled its potential as an indicator for various health issues, including liver disease, cardiovascular conditions, and metabolic syndrome [5-7]. While prior studies have examined its relevance in diagnosing different cancers like endometrial, lung, and liver cancer [8-10], the association between RDW and ovarian cancer remains unexplored. In this study, we investigate the correlation between RDW and hematological parameter in ovarian cancer by analyzing their variations.

MATERIAL AND METHODS:

Methodology: This retrospective longitudinal study aimed to assess hematological parameters in ovarian cancer patients attending the Obstetrics and Gynecology department at Mc Gann's Teaching District Hospital in Shivamogga. The study data was obtained from the Medical Records Department (MRD) of Mc Gann's Teaching District Hospital in Shivamogga. Patients presenting symptoms suggestive of ovarian cancer, such as abnormal uterine bleeding, abdominal discomfort, and weight loss was enrolled. Diagnostic procedures included abdominal and pelvic ultrasound for initial assessment, complemented by MRI and/or CT scans for further evaluation of suspected abnormalities. Confirmatory biopsies or surgical procedures were conducted, with histopathological analysis used for definitive diagnosis and determination of ovarian cancer subtype. The data collected encompassed various hematological parameters including RDW, platelet counts, neutrophil count, monocyte count, basophil count, and lymphocyte count. Additionally, ratios such as NLR (Neutrophil-to-Lymphocyte Ratio) and PLR (Platelet-to-Lymphocyte Ratio) were also included. Histopathology reports of tissue samples were available and conducted according to CAP (College of American Pathologists) protocol.

Inclusion and Exclusion Criteria: Inclusion criteria are patients who are diagnosed as having malignancy in ovary or presence of benign ovarian tumor or subjects without any of this condition.

Patients were excluded if they had previously known kidney diseases (CKD, SLE and polycystic kidney, renal calculi), known malignant disease, anemia, recent iron therapy or recent blood transfusion and any acute illness.

Study Subjects: The study consists of a cancer group comprising 13 individuals with ovarian cancer and benign group comprising of 26 individuals with non-malignant conditions/ benign ovarian tumors and a matched control group of 16 individuals without any signs and symptoms of cancer or benign condition

RESULTS: Table 1 presents the demographic characteristics of the study population, including mean values and standard deviations (SD), alongside the results of the analysis of variance (ANOVA). For RDW, PLR, and NLR, the values were notably higher in the Case group compared to both the Controls and Normal groups. RDW was approximately 34% higher in the Case group compared to Controls and 15% higher compared to Normal. PLR was about 90% higher in the Case group than Controls and 46% higher than Normal. Similarly, NLR was approximately 103% higher in the Case group compared to Controls and 20% higher than Normal.

ANOVA was utilized to evaluate the impact of hematological parameters across distinct conditions. The analysis uncovered significant disparities in several parameters. Specifically, Red Cell Distribution Width (RDW) displayed a noteworthy difference ($p = 0.033$), primarily evident between the case and control groups. Moreover, Platelet-to-Lymphocyte Ratio (PLR), Neutrophil-to-Lymphocyte Ratio (NLR), Lymphocyte count (L), and Neutrophil count (N)

also exhibited significant differences (p = 0.004, p = 0.001, p = 0.0006, p = 0.003 respectively). Post hoc analysis highlighted significant distinctions between the case and control groups for PLR, NLR, L, and N parameters (p = 0.003, p = 0.002, p = 0.001, p = 0.005 respectively). Additionally, a significant discrepancy in Lymphocyte count (L) was noted between the control and normal groups (p = 0.03). Nevertheless, Platelet count, Basophil count, Eosinophil count, and Monocyte count did not demonstrate any significant variations among the groups.

TABLE 1: SHOWS THE DEMOGRAPHIC DATA OF THE STUDY POPULATION IN MEAN AND SD

	Case (13)	Controls (26)	Normal (16)	p value
Age in yrs	52.23 ± 10.76	41.46 ± 15.66	44.12 ± 12.03	0.075
RDW	19.86 ± 9.64	14.82 ± 2.40	17.34 ± 4.96	0.033*
PLR	0.19 ± 0.09	0.10 ± 0.06	0.13 ± 0.05	0.004**
NLR	4.45 ± 2.12	2.19 ± 1.42	3.71 ± 2.14	0.001***
N	71.86 ± 9.22	58.55 ± 13.17	67.76 ± 11.67	0.003**
L	18.73 ± 6.32	33.41 ± 13.98	22.97 ± 9.49	0.0006***
M	4.56 ± 3.52	5.42 ± 3.00	5.66 ± 1.65	0.55
E	4.53 ± 3.14	4.64 ± 2.68	3.14 ± 3.21	0.25
B	0.3 ± 0.47	0.45 ± 0.61	0.41 ± 0.24	0.65
Platelet	3.36 ± 1.36	3.09 ± 0.82	2.83 ± 0.62	0.32

Table 2 displays the correlation between RDW and various blood parameters in cancer subjects. RDW shows a significant negative correlation with lymphocytes (Ly) (r = -0.54, p = 0.05) and eosinophils (Eo) (r = -0.55, p = 0.05). No significant correlations were observed for other parameters. For the control and normal groups, no significant correlations were observed between RDW and any of the blood parameters.

TABLE 2: SHOWS CORRELATION BETWEEN THE BLOOD PARAMETERS AND RDW IN THE CANCER SUBJECTS

Correlation of RDW with	R	p value
Plt	-0.43	0.13
PLR	-0.031	0.91
NLR	-0.39	0.18
Ne	-0.14	0.65
Ly	-0.54	0.05*
Mo	-0.12	0.68
Eo	-0.55	0.05*
Ba	-0.059	0.84

DISCUSSION: Red Cell Distribution Width (RDW) stands as a cost-effective, easily accessible, and non-invasive standard biomarker, indicating a significant disturbance in erythrocyte homeostasis. Its straightforward measurement offers essential insights into red blood cell size variability, enhancing the evaluation of diverse health conditions [10-13]. This simplicity and cost-effectiveness position RDW as a practical and efficient tool for widespread integration into routine clinical practices.

A more stable erythrocyte population indicates balanced erythropoiesis and homeostasis. Hence a higher value is seen in normal subject when compared with the benign condition. In our investigation, a noteworthy finding was the discernible difference in RDW levels between cancer condition and those with benign conditions. This discrepancy suggests a potential link to underlying mechanisms. Conversely, malignant conditions may disrupt this equilibrium, resulting in a slight elevation in RDW due to altered erythrocyte dynamics. Malignant conditions may can still cause some degree of variation like inflammation, nutritional deficiencies and other physiological changes. This observation underscores the sensitivity of RDW to changes in erythrocyte homeostasis which, is an indicative of cancer, still impact erythrocyte dynamics and subsequently affect RDW and emphasizes its potential as a valuable indicator for discerning variations in health conditions.

Further elevated RDW levels were observed in ovarian cancer subjects compared to those with benign and normal conditions. This implies that RDW may serve as a valuable marker for identifying cancer, substantiating earlier research demonstrating heightened RDW levels in individuals with cancer [14]. The initial mechanism involves the fact that malignant tumors are often associated with a systemic inflammatory response. Malignant tumors release pro-inflammatory mediators, inducing immune responses and inflammation, thereby stimulating acute-phase proteins. The resultant systemic inflammatory response impacts hematopoiesis, altering blood parameters like RDW. Elevated RDW levels reflect the ongoing inflammation linked with malignant tumors. Thus RDW acts as an inflammatory marker, as evidenced by its positive association with various inflammation biomarkers in several studies across different conditions [15-17]. This interplay highlights the intricate relationship between cancer, inflammation, and RDW, emphasizing RDW's potential role as a dynamic indicator of the inflammatory state in cancer patients.

The Neutrophil to Lymphocyte Ratio (NLR) serves as a marker reflecting inflammation and immune response by calculating the ratio of absolute neutrophil count to lymphocyte count in peripheral blood. Within the tumor microenvironment, an increased NLR indicates both neutrophilia and lymphopenia[18]. This imbalance supports cancer cell invasion, migration, and angiogenesis, contributing to cancer progression. Meanwhile, the decline in lymphocytes signifies an inadequate immune response to the tumor which is observed in our study[19]. This intricate interplay between neutrophils and lymphocytes highlights the role of NLR in gauging the dynamic host-tumor interaction, providing valuable insights into cancer pathogenesis and progression.

In a study by Raungkaewmanee *et al* which evaluated platelet count and Neutrophil-to-Lymphocyte Ratio (NLR) alongside Platelet-to-Lymphocyte Ratio (PLR) to compare their effectiveness in predicting advanced stage of ovarian cancer and post-surgery residual disease [20]. Though these factors exhibited modest predictive values, PLR demonstrated superior performance among them. Even in a subgroup with advanced stage disease, PLR maintained a robust ability to determine surgical outcomes and residual disease. This underscores the potential utility of PLR as a valuable prognostic indicator in such clinical scenarios. However, in our study it suggests that higher NLR values are associated with the "case" group compared to both "control" and "normal" groups.

CONCLUSION: In summary, Red Cell Distribution Width (RDW) proves to be a cost-effective marker, showcasing notable distinctions between cancer and benign conditions. Elevated RDW levels in ovarian cancer subjects underscore its potential as a valuable cancer marker, in line with previous research on its association with inflammatory states. The Neutrophil-to-Lymphocyte Ratio (NLR) emerges as a vital marker reflecting inflammation and immune response, offering insights into cancer pathogenesis. Although Platelet-to-Lymphocyte Ratio (PLR) outperformed in predicting advanced ovarian cancer stages in prior studies, our findings emphasize the significance of higher NLR values in the "case" group, highlighting its dynamic role in clinical scenarios. Also these markers can be used as prognostic indicators and to monitor the therapy.

ACKNOWLEDGEMENT: Authors acknowledge Rajiv Gandhi University of Health Sciences, Karnataka, Department of Pathology, Department of Gynecology and Obstetrics and Multidisciplinary Research Unit for their support in conducting this study.

Funding: This work was supported by the grant from Rajiv Gandhi University of Health Sciences, Karnataka, STS Project Code: UG23MED272, Approved in FY 2023-24.

Ethical Approval: The study was approved by the Institutional Ethics Committee, Shimoga Institute of Medical Science, Shivamogga, Ref. No.: SIMS/IEC/878/2022-23.

CONFLICT OF INTEREST: None declared.

REFERENCES:

1. GLOBOCAN 200Estimated cancer Incidence, Mortality, Prevalence and Disability-adjusted life years (DALYs). Worldwide in 2008. http://globocan.iarc.fr/.: s.n.

2. Danforth KN, Im TM and Whitlock EP: Addendum to Screening for Ovarian Cancer: Evidence Update for the US Preventive Services Task Force Reaffirmation Recommendation Statement. AHRQ Publication No. 12-05165-EF4. Rockville, MD: Agency for Healthcare Research and Quality April 2012.
3. Murthy NS, Shalini S and Suman G: Changing trends in incidence of ovarian cancer – the Indian scenario. Asian Pac J Cancer Prev 2009; 10: 1025-30.
4. Siegel R, Naishadham D and Jemal A: Cancer statistics, 2013. CA Cancer J Clin 2013; 63: 11–30.
5. Siegel R, Naishadham D and Jemal A: Cancer statistics, 2012. CA Cancer J Clin 2012; 62: 10–29.
6. Torre LA, Bray F and Siegel RL: Global cancer statisitics, 2012. CA Cancer J Clin 2015; 65: 87–108.
7. Dong X, Men X and Zhang W: Advances in tumor markers of ovarian cancer for early diagnosis. Indian J Cancer 2014; 51(3): 72– 6.
8. Evans TC and Jehle D: The red blood cell distribution width. J Emerg Med 1991; 9(1): 71–4.
9. Hu Z, Sun Y and Wang Q: Red blood cell distribution width is a potential prognostic index for liver disease. Clin Chem Lab Med 2013; 51: 1403–8.
10. Montagnana M, Cervellin G and Meschi T: The role of red blood cell distribution width in cardiovascular and thrombotic disorders. Clin Chem Lab Med 2011; 50: 635–41.
11. Salvagno GL, Sanchis-Gomar F, Picanza A and Lippi G: Red blood cell distribution width: a simple parameter with multiple clinical applications. Critical Reviews in Clinical Laboratory Sciences 2015; 52(2): 86-105.
12. Hu L, Li M, Ding Y, Pu L, Liu J, Xie J, Cabanero M, Li J, Xiang R and Xiong S: Prognostic value of RDW in cancers: a systematic review and meta-analysis. Oncotarget 2017; 8(9): 16027.
13. Malandrino N, Wu WC, Taveira TH, Whitlatch HB and Smith RJ: Association between red blood cell distribution width and macrovascular and microvascular complications in diabetes. Diabetologia 2012; 55: 226-35.
14. Qin Y, Wang P, Huang Z, Huang G, Tang J, Guo Y, Huang P, Lai Z and Lin F: The value of red cell distribution width in patients with ovarian cancer. Medicine 2017; 96(17).
15. Horta-Baas G and Romero-Figueroa MD: Clinical utility of red blood cell distribution width in inflammatory and non-inflammatory joint diseases. International Journal of Rheumatic Diseases 2019; 22(1): 47-54.
16. He Y, Liu C, Zeng Z, Ye W, Lin J and Ou Q: Red blood cell distribution width: a potential laboratory parameter for monitoring inflammation in rheumatoid arthritis. Clinical Rheumatology 2018; 37: 161-7.
17. Lippi G, Targher G, Montagnana M, Salvagno GL, Zoppini G and Guidi GC: Relation between red blood cell distribution width and inflammatory biomarkers in a large cohort of unselected outpatients. Archives of Pathology & Laboratory Medicine 2009; 133(4):
18. Powell DR and Huttenlocher A: Neutrophils in the tumor microenvironment. Trends in Immunology 2016; 37(1): 41-52.
19. Baert T, Van Camp J, Vanbrabant L, Busschaert P, Laenen A, Han S, Van Nieuwenhuysen E, Vergote I and Coosemans A: Influence of CA125, platelet count and neutrophil to lymphocyte ratio on the immune system of ovarian cancer patients. Gynecologic Oncology 2018; 150(1): 31-7.
20. Raungkaewmanee S, Tangjitgamol S, Manusirivithaya S, Srijaipracharoen S and Thavaramara T: Platelet to lymphocyte ratio as a prognostic factor for epithelial ovarian cancer. Journal of Gynecologic Oncology 2012; 23(4): 265-73.

How to cite this article:
Bhaktha G, Shetty A and Veena S: Red cell distribution width assessment and hematological correlation in ovarian cancer. Int J Pharm Sci & Res 2024; 15(9): 2722-26. doi: 10.13040/IJPSR.0975-8232.15(9).2722-26.