Original Article

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Website: https://journals.lww.com/ijhm

DOI: 10.4103/ijh.ijh_2_25

Assessment of red cell distribution width in patients with hematological malignancy

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Abstract:

BACKGROUND: Red cell distribution width (RDW) is one of the red cell parameters. It reflects the variation in the size and shape of red blood cells (RBCs). It changes in different disease processes. It has a role in evaluating the prognosis in patients with different cancer types, including hematological malignancies, reflecting the effect of inflammatory cytokines produced by malignant cells on the shape and size of RBC. In general, cancer-associated inflammation represents the hallmark of cancer development and progression. Based on these facts, many studies evaluate the role of RDW in the prognosis. RDW is associated with cancer-induced malnutrition and malabsorption, which causes hematinic deficiency, reflecting its correlation with poor prognosis. Furthermore, higher RDW is associated with higher cardiovascular and inflammatory risks, thus increasing the risk of chemotherapy-induced cardiotoxicity.

OBJECTIVES: We assess the difference between RDW from healthy people and patients diagnosed with hematological malignancies.

MATERIALS AND METHODS: This study was performed in Babylon Province, comparing the RDW difference between healthy people and hematological malignancy patients. A total of 148 participants, 74 of them were healthy people and 74 were newly diagnosed with hematological malignancies, 44 with myeloid malignancy, 30 with lymphoid malignancy.

RESULTS: The mean RDW-coefficient of variation (CV) for healthy people was 13.33 ± 1.14, whereas that for patients was 16.12 ± 3.62 with a significant difference ($P < 0.0001$). Similarly, the mean RDW-standard deviation (SD) for healthy people was 45.01 ± 4.96, whereas that for patients was 57.10 ± 12.78 with a significant difference ($P < 0.0001$). Similarly, there is a significant difference in RDW-SD and RDW-CV between those with myeloid and lymphoid neoplasms as separately compared to healthy people ($P < 0.0001$). However, a significant difference was only found in RDW-CV in comparison between these two groups ($P = 0.04$).

CONCLUSION: Measurement of RDW of both types is important for predicting the prognosis of hematological malignancies. However, it is limited to the determination of the significant difference in RDW between healthy people and patients who are newly diagnosed with hematological malignancies without studying RDW effect on disease prognosis.

Keywords:

Hematological malignancy, red cell distribution width-coefficient of variation, red cell distribution width-standard deviation

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Submission: 03-01-2025
Revised: 23-02-2025
Accepted: 07-03-2025
Published: 24-04-2025

Introduction

Red cell distribution width (RDW) is one of the red blood cell (RBC) parameters measured by the complete blood count (CBC) test. It reflects the variation in the size and shape of RBCs.[1] A great attention was paid to its changes in different disease processes, including cardiovascular, thrombotic, hepatic, and renal failure, in addition to its role in benign RBC disorders

How to cite this article: Gatea AK, Al-Jabory MA, Shamki BA, Al-Sabary AH. Assessment of red cell distribution width in patients with hematological malignancy. Iraqi J Hematol 2025;14:32-6.

such as iron deficiency anemia and thalassemia.[1] More recently, it has had a role in evaluating the prognosis in patients with different cancer types, such as lung, colorectal, breast, and pancreatic cancers, as well as different hematological malignancies.[2] RDW measurement includes two indices: RDW-coefficient of variation (CV) and RDW-standard deviation (SD).[3] RDW is calculated as a ratio by multiplying one SD of RBC volume by the mean cell volume (MCV) by 100, and this is called RDW-CV.[3] Nowadays, automatic blood analyzers can measure different types of RDW in the CBC.[4] Unlike RDW-CV, RDW-SD is not a ratio, and it represents the direct measure of the distribution curve of RBC volume at the level 20% above the baseline.[4] RDW-SD eliminates the influence of MCV from RDW and reflects the variation in RBC shape, whereas RDW-CV reflects the variation in both the size and the shape. For this reason, RDW-SD is superior to RDW-CV in evaluating poikilocytosis.[4]

Hematological malignancies, including acute and chronic leukemias, lymphomas, myeloproliferative neoplasms, and multiple myeloma, are among the most common cancers worldwide.[5] Its burden is higher in men than in women, reflecting the higher exposure of men to occupational and environmental hazards; different countries have different incidences of different types of hematological malignancies due to different socioeconomic developmental stages.[5] Hematological malignancies have multiple effects on RBC indices measured by the CBC, including RDW, reflecting the effect of inflammatory cytokines produced by malignant cells on the shape and size of RBC.[6] In general, cancer-associated inflammation represents the hallmark of cancer development and progression, and this can affect the level of different inflammatory markers, including C-reactive protein (CRP) and erythrocyte sedimentation rate. Based on these facts, many studies evaluate the role of RDW in the prognosis of different cancer types, including hematological ones, but the mechanism remains unclear.[7] Other inflammatory markers, including interleukin-6, tumor necrosis factor, and soluble transferrin receptors, were also associated with changes in RDW, possibly explaining their effect on erythropoiesis, which resulted in changes in RBC maturation and, subsequently, RDW.[6] Another explanation is that RDW is associated with cancer-induced malnutrition and malabsorption, which causes hematinic deficiency (iron, B12, and folate), reflecting its correlation with poor prognosis.[6,7] Another important point to focus on is that higher RDW is associated with higher cardiovascular and inflammatory risks, thus increasing the risk of chemotherapy-induced cardiotoxicity.[8] In this study, we assess the difference between RDW from healthy people and patients diagnosed with hematological malignancies.

Materials and Methods

This is a cross-sectional study conducted for 2 months from the beginning of March to end of April 2024 in Babylon Province in Al-Imam Al-Sadiq General Hospital, Clinical Hematology Department, comparing the RDW difference between healthy people and hematological malignancy patients. A total of 148 participants, 74 of them were healthy people and 74 were diagnosed with different hematological malignancies, 44 with myeloid malignancy (24 had acute myeloid leukemia, 11 had myeloproliferative neoplasm, 5 had chronic myeloid leukemia [CML], 2 had myelodysplastic syndrome, and 1 had chronic myelomonocytic leukemia), 30 with lymphoid malignancy (16 had lymphoma, 7 had multiple myeloma, 5 had acute lymphoblastic leukemia, and 2 had chronic lymphocytic leukemia). After obtaining consent, blood was sampled for CBC assessment using five differential hematology autoanalyzers, Mindray BC-5000, China.

Statistical analysis

Comparison between diseased and healthy group parameters using t-test analysis by SPSS v25, (IBM, New York, USA). With $P \leq 0.05$ was considered statistically significant

Ethical approval

This study was approved by the research ethics committee at Hammurabi College of Medicine, by document No. 1483 on March 13, 2024.

Results

The criteria of the study participants (healthy people and hematological malignancy patients) are shown in Table 1. The mean RDW-CV for healthy people was 13.33 ± 1.14, whereas that for hematological malignancy patients was 16.12 ± 3.62, with a significant difference between the two groups ($P < 0.0001$). Similarly, the mean RDW-SD for healthy people was 45.01 ± 4.96, whereas that for

Table 1: Criteria of the study participants

Criteria	Healthy people	Hematological malignancy patients	*P*
n	74	74	
Age (years), mean±SD	44.01±15.32	46.87±17.97	0.3
Female	49	37	
Male	26	38	
RDW-CV (fL), mean±SD	13.33±1.14	16.12±3.62	<0.0001
RDW-SD (fL), mean±SD	45.01±4.96	57.10±12.78	<0.0001
WBC (×10^9/L), mean±SD	7.404±2.19	23.99±49.78	0.045
Hb (g/dL), mean±SD	13.27±1.39	11.16±2.80	0.001
Platelet (×10^9/L), mean±SD	277.13±67.23	244.87±216.38	0.5

Hb=Hemoglobin, WBC=White blood cell, SD=Standard deviation, RDW-SD=Red cell distribution width-SD, RDW-CV=Red cell distribution width-coefficient of variation

hematological malignancy patients was 57.10 ± 12.78, with a significant difference between the two groups ($P < 0.0001$).

The patient group was divided into myeloid and lymphoid malignancy (44 and 30, respectively). There is a significant difference between the two groups in RDW-CV with no significant change in RDW-SD. They also have significant differences in both RDW-SD and RDW-CV from healthy people, with their criteria as shown in Tables 2-4.

Table 2: Criteria of myeloid versus lymphoid participants

Criteria	Myeloid	Lymphoid	*P*
n	44	30	
Age (years), mean±SD	43.32±17.19	52.13±18.37	0.04
Female	18	19	
Male	26	11	
RDW-CV (fL), mean±SD	16.72±4.05	15.05±2.52	0.04
RDW-SD (fL), mean±SD	58.61±14.31	55.79±9.08	0.3
WBC (×10^9/L), mean±SD	27.23±56.37	14.46±28.21	0.25
Hb (g/dL), mean±SD	11.22±3.17	11.11±2.26	0.9
Platelet (×10^9/L), mean±SD	258.75±259.27	228.35±136.98	0.5

Hb=Hemoglobin, WBC=White blood cell, SD=Standard deviation, RDW-SD=Red cell distribution width-SD, RDW-CV=Red cell distribution width-coefficient of variation

Table 3: Criteria of myeloid versus normal participants

Criteria	Healthy people	Myeloid	*P*
n	74	44	
Age (years), mean±SD	44.01±15.32	43.32±17.19	0.82
Female	49	18	
Male	26	26	
RDW-CV (fL), mean±SD	13.33±1.14	16.72±4.05	<0.0001
RDW-SD (fL), mean±SD	45.01±4.96	58.61±14.31	<0.0001
WBC (×10^9/L), mean±SD	7.404±2.19	27.23±56.37	0.003
Hb (g/dL), mean±SD	13.27±1.39	11.22±3.17	0.0001
Platelet (×10^9/L), mean±SD	277.13±67.23	258.75±259.27	0.56

Hb=Hemoglobin, WBC=White blood cell, SD=Standard deviation, RDW-SD=Red cell distribution width-SD, RDW-CV=Red cell distribution width-coefficient of variation

Table 4: Criteria of lymphoid versus normal participants

Criteria	Healthy people	Lymphoid	P
n	74	30	
Age (years), mean±SD	44.01±15.32	52.13±18.37	0.02
Female	49	19	
Male	26	11	
RDW-CV (fL), mean±SD	13.33±1.14	15.05±2.52	<0.0001
RDW-SD (fL), mean±SD	45.01±4.96	55.79±9.08	<0.0001
WBC (×10^9/L), mean±SD	7.404±2.19	14.46±28.21	0.03
Hb (g/dL), mean±SD	13.27±1.39	11.11±2.26	0.0001
Platelet (×10^9/L), mean±SD	277.13±67.23	228.35±136.98	0.95

Hb=Hemoglobin, WBC=White blood cell, SD=Standard deviation, RDW-SD=Red cell distribution width-SD, RDW-CV=Red cell distribution width-coefficient of variation

Discussion

Hematological malignancies represent a major health burden worldwide. They are caused by impaired hematopoiesis, including myeloid and lymphoid subtypes. With increasing cancer cases, hematological malignancies are also increasing, and their spectrum is also changing, but the mortality rate is decreasing due to earlier detection of the disease, and advancing investigational and therapeutic facilities.[5] In this study, we assess the benefit of one of the important and already available blood parameters called RDW in patients diagnosed with hematological malignancies. The results showed a significant difference between healthy people with normal CBC and patients newly diagnosed with different types of hematological malignancies in many hematological parameters, including RDW. Similarly, a significant difference in RDW between those with myeloid and lymphoid neoplasms as separately compared to healthy people. However, a significant difference was only found in RDW-CV (without RDW-SD) in comparison between these two patient groups. Comparable results were obtained by many other studies worldwide. In lymphoid malignancies, Chrobák *et al*. evaluate the role of RDW in patients with hairy cell leukemia, revealing that high RDW is associated with active disease and is reversible after successful treatment.[9] Lee *et al*. demonstrated that multiple myeloma patients with higher RDW have poorer prognosis and more advanced disease than those who had normal RDW.[10-12] Another two studies evaluating the role of RDW in patients diagnosed with diffuse large B-cell lymphoma revealed that those who have higher RDW were associated with worse event-free survival, overall survival (OS), and associated with both higher CRP and low albumin, which support the effect of inflammation and malnutrition on RDW level.[13,14]

RDW was combined with the International Prognostic Index, Korean Prognostic Index, and prognostic index of natural killer lymphoma in a study done by Luo *et al*., which revealed that this combination showed a more powerful prognostic value than the original models.[15] On the other hand, a study performed by Podhorecka *et al*. suggests that higher RDW is an independent predictor of shorter survival but has no correlation with disease progression in CLL patients.[16] Regarding Hodgkin lymphoma (HL), RDW was affecting progression-free survival, OS and was found to have a strong connection with most of the prognostic factors in HL, and surprisingly, there was a relationship with long-term development of secondary malignancies, which represent a critical adverse prognostic factor in HL.[2]

In myeloid malignancies, CML patients were studied by Iriyama *et al*., who found that patients with higher RDW

had a lower 5-year event and transformation-free survivals with a higher death rate.[17] Buckstein *et al*. developed a scoring system used for predicting the diagnosis of MDS in patients with cytopenia and macrocytosis, and this score includes four parameters (age, MCV, RDW, and lactate dehydrogenase) with a likelihood of diagnosis increasing from 12% to 48% when three or more factors present.[18] Baba *et al*. performed a study suggesting that higher RDW reflects the role of dyserythropoiesis in the pathophysiology of MDS without a significant correlation with MDS-related chromosomal abnormalities and those who have refractory anemia subtype have a poorer prognosis than those with refractory anemia with the excess blast.[19]

Regarding acute leukemia, a study conducted by Yaegashi *et al*. was the first one to assess the effect of RDW in acute myeloid leukemia (AML) patients, concluding that higher RDW level at the time of diagnosis was associated with many effects, including being diagnosed with secondary type AML, poorer cytogenetic risk stratification, worse outcome irrespective to other outcome affecting factors, and higher treatment-related morbidity and mortality, especially anthracycline-associated cardiotoxicity which can be explained by the presence of oxidative stress that induce bone marrow dysfunction resulting in impaired heme and subsequently hemoglobin synthesis leading to higher RDW.[8,20] Another study evaluating the role of RDW in predicting the outcome of allogenic BMT in acute leukemia patients revealed that those who have increased RDW-SD before transplant had a higher relapse rate thereafter.[21] Conversely, a study conducted among children diagnosed with ALL revealed no significant correlation between high RDW levels and both mortality and relapse rate, supporting the fact that RDW is highly affected by aging, inflammation, and oxidative stress seen among older patients diagnosed with malignancy.[22]

A meta-analysis study performed by Ai *et al*. concluded that hematological malignancies and many cancer patients with high RDW were associated with a poorer prognosis than those who have normal readings.[1,6]

Conclusion

Both RDW-CV and RDW-SD are changed in the newly diagnosed hematological cancer patients compared to healthy control. Further studies are required to predict its effect on disease prognosis and also the changes associated with treatment protocol. However, this study is limited to the determination of the significant difference in RDW between healthy people and patients diagnosed with hematological malignancies without studying RDW's effect on disease prognosis.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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