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Original Research

# Prognostic value of absolute lymphocyte/monocyte ratio, red cell distribution width and neutrophil/ lymphocyte ratio in diffuse large B-cell lymphoma patients

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**Abstract:** Diffuse large B-cell lymphoma (DLBCL) is an aggressive and rapid-growing form of non-Hodgkin lymphoma (NHL). The objective of this research was to assess the predictive role of lymphocyte to monocyte ratio (LMR), red cell distribution width (RDW) and neutrophil to lymphocyte ratio (NLR) values in the survival of DLBCL patients. A retrospective analysis of 136 DLBCL patients admitted to Nanakali Hospital for blood diseases and oncology from 2010-2020 was done. We assessed the correlation of LMR, RDW and NLR with patients' characteristics and the impact on survival by the Kaplan–Meier method, the log-rank test, and Cox regression models for multivariate analysis. The complete remission rate was 61.7%, with a 5- year overall survival (OS) and progression-free survival (PFS) of 59.5% and 60%, respectively. The Log-rank test showed that LMR was significantly correlated with Ann Arbor staging (p= 0.040). There is a significant association between RDW and Eastern Cooperative Oncology Group performance status (ECOG-performance status) (p= 0.022), B symptoms (p= 0.026), Revised International prognostic index (R-IPI) (p= 0.004), lactate dehydrogenase (LDH) (p= 0.021), and beta 2 microglobulin (B2MG) (p= 0.007), whereas NLR had a significant correlation with LDH only (p=0.016). There were no significant differences in the 5-year OS or PFS in patients with different levels of RDW, LMR, and NLR. LMR, RDW and NLR were correlated with many of patients' characteristics. However, none of the LMR, RDW and NLR did possess value to predict OS and PFS, and they cannot be used as biomarkers for survival evaluation of DLBCL.

***Key words:*** Diffuse large B cell lymphoma; Survival; Red cell distribution width; Lymphocyte-monocyte ratio; Neutrophil-lymphocyte ratio.

## Introduction

Diffuse large B-cell lymphoma (DLBCL) is an aggressive and rapid-growing form of non-Hodgkin lymphoma (NHL). It is the most usual type, accounting for about 30 to 40 percent of all adult NHLs, and more than 80% of aggressive lymphomas. Also, at the time of diagnosis, most patients are in advanced stages (1, 2). If left untreated, DLBCL is lethal, but for now, the rate of complete remission (CR) is 76–86 percent, with standard R-CHOP treatment (prednisone, vincristine, doxorubicin, cyclophosphamide and rituximab) (3-5). On the other hand, the five-year progression-free survival (PFS) and overall survival (OS) are only achievable in 58–70% of DLBCL patients treated with R-CHOP (6, 7).

The International prognostic index (IPI), and revised IPI (R-IPI) are standard indicators for the prognosis of patients with aggressive NHL (7-9) R-IPI includes the age of the patient ($\leq$60 years *versus* $>$60 years, clinical-stage Ann Arbor Stage (I/II *versus* III/IV), performance status (Eastern Cooperative Oncology Group [ECOG] 0, 1 *versus* $>$ 1), serum lactate dehydrogenase (LDH) level ($\leq$ upper limit of normal [ULN] *versus* $>$ ULN) and the number of extranodal (EN) lesions (0, 1 *versus* $>$ 1). R-IPI groups the DLBCL patients into three prognostic groups; "very good, good and poor-risk groups" with long-term PFS of (90%, 80%, and 50% respectively).

However, despite being good prognostic indexes, the IPI and the R-IPI do not detect a risk group with less than a 50% survival chance. Even the R-IPI is not able to detect patients who have a survival chance of less than 60% in three years (10). Therefore, to recognize those patients at high risk of the failure of standard treatment (rituximab (R) and cyclophosphamide, doxorubicin, vincristine, prednisone (R-CHOP), who in need of alternate therapies, other predictors were determined like a biological marker (11), gene profile (12), and complete cell count (CBC) as well due to its prognostic impact in the treatment of DLBCL (13-15). LMR may reflect the interaction between the host immunity (lymphocytes) and tumor microenvironment (monocytes), denoting that the clinical outcomes of lymphomas are correlated with tumor inflammation and immunology. Low LMR at diagnosis may be related to a more aggressive disease nature or lower tolerance to anti-cancer treatment (16). Recent studies showed that baseline LMR can predict the disease outcome in certain hematological malignancies like DLBCL, and NK/T cell lymphoma (17, 18).

Lymphopenia and monocyte and neutrophil count were identified to have prognostic value in DLBCL (14,

15, 19, 20).

Red cell distribution width (RDW) which is representing the volume variation of red blood cells and is routinely measured as part of CBC has a significant role in tumor progression and prognosis (21, 22). Some researches and a meta-analysis showed that RDW is a potent predictor of all-cause mortality, such as cancer-related deaths (23, 24).

The study aimed to find the association between certain baseline complete cell count parameters including LMR, NLR and RDW and some clinical and laboratory characteristics of DLBCL patients to detect their role in predicting total survival and progression-free survival.

## Materials and Methods

### Patients and methods

A total of 136 patients with DLBCL were included retrospectively, they were admitted to Nanakaly hospital for blood diseases and oncology (Erbil- Kurdistan Region of Iraq) during 2010-2020, all of them had lymph node biopsy for histopathology and immunohistochemistry studies. Additionally, hematological tests like complete blood picture (CBP) and erythrocyte sedimentation rate (ESR) were conducted for all patients. The absolute neutrophil count (ANC) with both lymphocyte/ monocyte ratio (LMR) and neutrophil/ lymphocyte ratio (NLR), absolute monocyte count (AMC), absolute lymphocyte count (ALC) and baseline RDW of patients was achieved. Besides, there were LDH and beta 2 microglobulin (B2MG). Also, radiological imaging like chest X-ray, ultrasound, whole-body computed tomography (CT) was used in all cases, and or positron emission tomography (PET-CT Scan) for many patients when it was available. CT and or PET- scans were used as initial baseline evaluation and for assessment of response to treatment as well. In addition, some characteristics such as sex, age, B symptoms, Ann Arbor stage, ECOG performance status (ECOG- PS) and the number of extranodal sites (EN) were determined. All patients were treated with R-CHOP protocol 6-8 cycles, with or without radiotherapy, in addition, some received high-dose methotrexate.

The response to treatment and the outcome of the disease (complete remission, refractory, relapse, or death) were recorded, PFS and OS were estimated. The study was approved by the Scientific and Ethical Committees of the College of Medicine, Hawler Medical University, Erbil-Iraq.

Those patients who have incomplete data refused chemotherapy, no proper follow-up and those with primary central nervous system DLBCL were excluded from this study.

The Statistical Package for the Social Science (SPSS 22, IBM, Armonk, NY, USA) was used for data analysis. The Chi-square test of association was used to compare proportions. The OS and PFS 5-year estimates were calculated using the life table method. Through the Kaplan–Meier method, survival curves were plotted. To demonstrate whether there was a significant difference in the survival of the study groups, the log-rank test (by Mantel-Cox) was applied. For multivariate analysis, Cox regression models were applied. A $P \leq 0.05$ was considered statistically significant.

## Results

### Patients' characteristics

The study comprised 136 DLBCL patients, ninety-two (67.6%) of them were male, with a female to male ratio (1:2.09). The median age was 51 years (range 15 to 81 years), and 38 patients (27.9%) were > 60 years old. Fifty-six patients (41.1%) were in the advanced Ann Arbor stage (III and IV) and about two-thirds of them (64.7%) had B symptoms (fever, night sweats, and weight loss) at the time of diagnosis. An ECOG PS ≥ 2 was identified in 49 patients (36%), and half of the patients (53.6%) had a good R-IPI score.

The mean LMR±SD was 6.27±4.97, the mean RDW±SD was 14.79±2.30, and the mean NLR±SD was 4.06±4.19. The rest of the clinical and some laboratory characteristics are shown in (Table 1). The follow-up period from diagnosis ranged from 3 to 133 months, with a median period of 35 months. The CR rate was 61.7%, with a 5-year OS and PFS of (59.5% and 60% respectively).

There was a significant association of LMR, RDW and NLR with some of the patients' characteristics. LMR was significantly correlated with Ann Arbor staging (p= 0.040), while RDW associated significantly with ECOG PS (p= 0.022), B symptoms (p= 0.026), R-IPI (p= 0.004), LDH (p= 0.021) and B2MG (p= 0.007), and NLR was significantly correlated with LDH (p=0.016) (Table 1).

### Receiver operating curve (ROC) analysis

Based on a ROC analysis of LMR, the patients were divided into low- and high- LMR groups through a cut-off value of 5.1%. The area under the curve (AUC) for LMR was 0.528 (95% confidence interval [CI] = 0.424–0.633), and the optimal cutoff value was 5.1%, with 52.2% sensitivity and 57.3% specificity (*P*=0.529; Figure 1A). There were 73 patients with a low LMR (< 5.1%) and 63 patients with a high LMR (≥ 5.1%).

According to the ROC analysis of RDW, the patients were divided into low- and high-RDW groups through a cutoff value of 14.85%. The AUC for RDW was 0.623 (95% CI = 0.526–0.719), and the optimal cutoff value was 14.8%, with 57.4% sensitivity and 62.9% specificity (*P*=0.019; Figure 1B). There were 76 patients with a low RDW (< 14.85%) and 60 patients with a high RDW (≥ 14.85%).

ROC analysis of NLR, the patients were divided into low- and high- NLR groups using a cutoff value of 2.8. The AUC for NLR was 0.512 (95% CI = 0.408–0.617), and the optimal cutoff value was 2.8, with 57.4% sensitivity and 55.1% specificity (*P*=0.812; Figure 1C). There were 69 patients with a low NLR (< 2.8) and 67

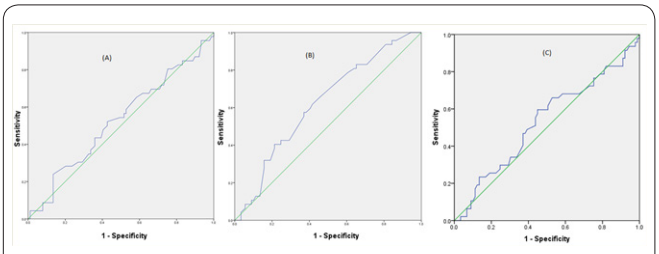


**Figure 1.** ROC curve for LMR (A), RDW (B), and NMR (C).

**Table 1.** Patients' baseline characteristics in relation to LMR, RDW and NLR levels.

| Factors | Total no. | Low LMR | | High LMR | | P-value | Low RDW | | High RDW | | P value | Low NLR | | High NLR | | P value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. | (%) | No. | (%) | | No. | (%) | No. | (%) | | No. | (%) | No. | (%) | |
| **Age** | | | | | | | | | | | | | | | | |
| ≤60 years | 98 | 57 | (58.2) | 41 | (41.8) | 0.092 | 55 | (56.1) | 43 | (43.9) | 0.928 | 52 | (53.1) | 46 | (46.9) | 0.384 |
| >60 years | 38 | 16 | (42.1) | 22 | (57.9) | | 21 | (55.3) | 17 | (44.7) | | 17 | (44.7) | 21 | (55.3) | |
| **Gender** | | | | | | | | | | | | | | | | |
| Male | 92 | 54 | (58.7) | 38 | (41.3) | 0.090 | 51 | (55.4) | 41 | (44.6) | 0.879 | 50 | (54.3) | 42 | (45.7) | 0.223 |
| Female | 44 | 19 | (43.2) | 25 | (56.8) | | 25 | (56.8) | 19 | (43.2) | | 19 | (43.2) | 25 | (56.8) | |
| **ECOG** | | | | | | | | | | | | | | | | |
| <2 | 87 | 48 | (55.2) | 39 | (44.8) | 0.641 | 55 | (63.2) | 32 | (36.8) | 0.022 | 43 | (49.4) | 44 | (50.6) | 0.684 |
| ≥2 | 49 | 25 | (51.0) | 24 | (49.0) | | 21 | 42.9) | 28 | (57.1) | | 26 | (53.1) | 23 | (46.9) | |
| **Ann arbor stage** | | | | | | | | | | | | | | | | |
| 1 | 38 | 15 | (39.5) | 23 | (60.5) | 0.040 | 27 | (71.1) | 11 | (28.9) | 0.130 | 21 | (55.3) | 17 | (44.7) | 0.559 |
| 2 | 42 | 25 | (59.5) | 17 | (40.5) | | 23 | (54.8) | 19 | (45.2) | | 19 | (45.2) | 23 | (54.8) | |
| 3 | 31 | 22 | (71.0) | 9 | (29.0) | | 14 | (45.2) | 17 | (54.8) | | 14 | (45.2) | 17 | (54.8) | |
| 4 | 25 | 11 | (44.0) | 14 | (56.0) | | 12 | (48.0) | 13 | (52.0) | | 15 | (60.0) | 10 | (40.0) | |
| **EN lesion** | | | | | | | | | | | | | | | | |
| ≤1 | 119 | 64 | (53.8) | 55 | (46.2) | 0.948 | 68 | (57.1) | 51 | (42.9) | 0.433 | 60 | (50.4) | 59 | (49.6) | 0.846 |
| >1 | 17 | 9 | (52.9) | 8 | (47.1) | | 8 | (47.1) | 9 | (52.9) | | 9 | (52.9) | 8 | (47.1) | |
| **B symptoms** | | | | | | | | | | | | | | | | |
| No | 48 | 25 | (52.1) | 23 | (47.9) | 0.783 | 33 | (68.8) | 15 | (31.3) | 0.026 | 27 | (56.3) | 21 | (43.8) | 0.342 |
| Yes | 88 | 48 | (54.5) | 40 | (45.5) | | 43 | (48.9) | 45 | (51.1) | | 42 | (47.7) | 46 | (52.3) | |
| **R-IPI** | | | | | | | | | | | | | | | | |
| Poor | 28 | 15 | (53.6) | 13 | (46.4) | 0.947 | 13 | (46.4) | 15 | (53.6) | 0.004 | 14 | (50.0) | 14 | (50.0) | 0.425 |
| Good | 73 | 40 | (54.8) | 33 | (45.2) | | 35 | (47.9) | 38 | (52.1) | | 34 | (46.6) | 39 | (53.4) | |
| Very good | 35 | 18 | (51.4) | 17 | (48.6) | | 28 | (80.0) | 7 | (20.0) | | 21 | (60.0) | 14 | (40.0) | |
| **LDH** | | | | | | | | | | | | | | | | |
| ≤250 | 65 | 30 | (46.2) | 35 | (53.8) | 0.092 | 43 | (66.2) | 22 | (33.8) | 0.021 | 40 | (61.5) | 25 | (38.5) | 0.016 |
| >250 | 71 | 43 | (60.6) | 28 | (39.4) | | 33 | (46.5) | 38 | (53.5) | | 29 | (40.8) | 42 | (59.2) | |
| **B2MG** | | | | | | | | | | | | | | | | |
| ≤3 | 51 | 22 | (43.1) | 29 | (56.9) | 0.056 | 36 | (70.6) | 15 | (29.4) | 0.007 | 28 | (54.9) | 23 | (45.1) | 0.452 |
| >3 | 85 | 51 | (60.0) | 34 | (40.0) | | 40 | (47.1) | 45 | (52.9) | | 41 | (48.2) | 44 | (51.8) | |
| **LMR mean±SD** | | 2.97 | 1.24 | 10.15 | 4.92 | <0.001 | 6.45 | 4.93 | 6.04 | 5.06 | 0.638 | 7.62 | 5.34 | 4.88 | 4.14 | 0.001 |
| **RDW mean±SD** | | 14.93 | 2.14 | 14.62 | 2.48 | 0.441 | 13.24 | 1.10 | 16.76 | 1.88 | <0.001 | 14.66 | 2.48 | 14.93 | 2.11 | 0.491 |
| **NLR mean±SD** | | 5.32 | 5.17 | 2.43 | 1.30 | <0.001 | 3.84 | 3.95 | 4.16 | 4.39 | 0.662 | 1.82 | 0.617 | 6.21 | 4.96 | <0.001 |

**Table 2.** Overall survival and progression-free survival rates in relation to the risk factors.

| Characteristics | PFS | | | | OS | | | |
|---|---|---|---|---|---|---|---|---|
| | 5-year rate% | (95% CI) | | P value | 5-year rate% | (95% CI) | | P value |
| All patients | 60 | 51.8 | 68.2 | | 59.5 | 51.2 | 67.8 | |
| **Age** | | | | | | | | |
| ≤60 | 61.7 | 52.1 | 71.3 | 0.441 | 63.6 | 54.1 | 73.1 | 0.342 |
| >60 | 56.9 | 41.2 | 72.7 | | 49.2 | 33.3 | 65.1 | |
| **Gender** | | | | | | | | |
| Male | 62.0 | 52.1 | 71.9 | 0.209 | 61.4 | 51.4 | 71.3 | 0.334 |
| Female | 57.0 | 42.3 | 71.6 | | 54.8 | 40.1 | 69.5 | |
| **ECOG** | | | | | | | | |
| <2 | 70.0 | 60.4 | 79.7 | 0.010 | 73.2 | 63.9 | 82.5 | 0.001 |
| ≥2 | 42.1 | 28.3 | 55.9 | | 36.1 | 22.6 | 49.5 | |
| **Ann arbor stage** | | | | | | | | |
| I | 84.4 | 72.9 | 96.0 | | 73.5 | 59.4 | 87.5 | |
| II | 69.5 | 55.5 | 83.4 | <0.001 | 75.0 | 61.9 | 88.1 | 0.001 |
| III | 43.8 | 26.4 | 61.3 | | 51.3 | 33.7 | 68.8 | |
| IV | 47.4 | 27.9 | 67.0 | | 20.5 | 4.7 | 36.3 | |
| **EN lesion** | | | | | | | | |
| ≤1 | 64.0 | 55.4 | 72.7 | 0.084 | 62.8 | 54.2 | 71.5 | 0.263 |
| > 1 | 37.1 | 14.2 | 60.1 | | 36.9 | 14.0 | 59.9 | |
| **B symptoms** | | | | | | | | |
| No | 75.3 | 63.1 | 87.5 | 0.008 | 80.7 | 69.6 | 91.9 | 0.002 |
| Yes | 50.5 | 40.1 | 61.0 | | 48.7 | 38.2 | 59.1 | |
| **R-IPI** | | | | | | | | |
| Poor | 19.2 | 4.6 | 33.8 | | 19.4 | 4.7 | 34.0 | |
| Good | 69.2 | 58.6 | 79.8 | <0.001 | 69.0 | 58.3 | 79.6 | 0.001 |
| Very good | 75.1 | 60.8 | 89.4 | | 70.4 | 55.3 | 85.5 | |
| **LDH** | | | | | | | | |
| ≤250 | 67.7 | 56.4 | 79.1 | 0.239 | 67.5 | 56.1 | 78.9 | 0.101 |
| > 250 | 53.5 | 41.9 | 65.1 | | 52.4 | 40.8 | 64.0 | |
| **B2MG** | | | | | | | | |
| ≤3 | 76.2 | 64.5 | 87.9 | 0.017 | 67.9 | 55.1 | 80.7 | 0.272 |
| >3 | 49.6 | 39.0 | 60.2 | | 54.3 | 43.7 | 64.8 | |
| **Platelet count** | | | | | | | | |
| <150 x$10^9$/dl | 38.9 | 17.8 | 60.1 | 0.02 | 52.3 | 30.7 | 74.0 | 0.304 |
| ≥150 x$10^9$/dl | 65.3 | 54.3 | 76.2 | | 61.2 | 50.9 | 71.5 | |
| **LMR** | | | | | | | | |
| Low <5.1 | 58.0 | 46.7 | 69.3 | 0.826 | 64.1 | 53.1 | 75.1 | 0.261 |
| High ≥5.1 | 63.0 | 51.1 | 74.9 | | 54.9 | 42.6 | 67.2 | |
| **RDW** | | | | | | | | |
| Low <14.85% | 67.2 | 56.7 | 77.8 | 0.217 | 68.6 | 38.8 | 61.2 | 0.095 |
| High ≥14.85% | 52.7 | 40.1 | 65.4 | | 50.0 | 56.9 | 80.4 | |
| **NLR** | | | | | | | | |
| Low <2.8 | 61.8 | 47.3 | 76.4 | 0.418 | 63.6 | 50.4 | 76.9 | 0.425 |
| High ≥2.8 | 58.8 | 45.3 | 72.4 | | 56.0 | 43.0 | 69.0 | |

patients with a high NLR (≥ 2.8).

**The survival studies**

The log rank analysis showed PFS has a significant correlation with ECOG PS (p= 0.010), Ann Abor stage (p= 0.000), R-IPI (p= 0.000), B symptoms (p= 0.008), B2MG (p= 0.017) and platelet count (p= 0.02), while OS associated significantly with ECOG PS (p= 0.001), Ann Arbor stage (p= 0.001), R-IPI (p= 0.001) and B symptoms (p= 0.002) (Table 2).

The 5 years OS was insignificantly higher in patients with low LMR, RDW and NLR levels compared to those with higher levels (p= 0.261, p=0.095, p=0.425 respectively). Also, the 5-year PFS was insignificantly higher in patients with low RDW and low NLR; while, it was insignificantly lower in patients with low LMR (p=0.217, p=0.418, p= 0.825 respectively) (see Figure 2 and Table 2).

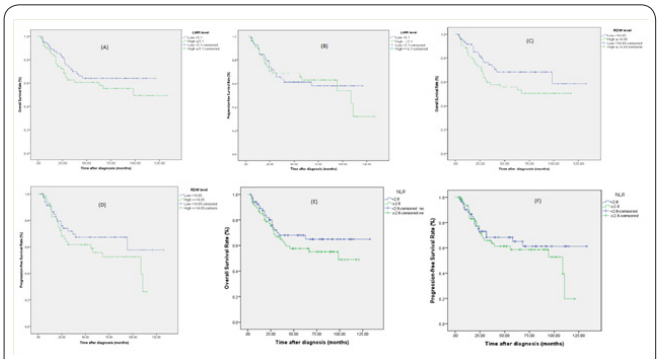

**Figure 2.** Correlation between overall survival with LMR (A), RDW (C), and NLR (E), and Correlation between 5-year progression-free survival with LMR (B), RDW (D), and NLR (F) (Kaplan-Meier survival analysis).

The multivariate Cox analysis showed a significant correlation between OS with Ann Arbor stage IV disease (Hazard Ratio (HR) of 6.556, p= 0.024), and EN lesion >1 (HR of 0.306, p= 0.043). The PFS was also significantly associated with stage IV (HR of 5.355, p= 0.032), EN lesion >1 versus EN lesion ≤ 1 (HR of 0.273, p= 0.032), R-IPI good category (HR of 0.140, p= 0.005) and patients with normal platelet count (HR of 0.325, p=0.005). Patients with lower LMR levels had a lower risk of death (HR= 0.728 (95% CI 0.366-1.451) and relapse (HR=0.906 (95%CI 0.413-1.986) than those with a higher LMR level, but this was not statistically significant (p=0.367, p=0.804 respectively). Patients with higher RDW levels had a higher risk of death (HR= 1.480 (95%CI 0.762-2.875) and relapse (HR=1.154 (95%CI 0.613-2.172) than those with a lower RDW level, but this was not statistically significant (p=0.247, p=0.657, respectively). In addition, we detected that patients with higher NLR levels had a higher risk of death (HR= 1.458 (95%CI 0.734-2.895)) and relapse rate (HR=1.198 (95%CI 0.584- 2.456)) than those with a lower NLR level, however, they were not significant (p=0.282, p=0.623 respectively). Details of multivariate Cox analysis results are shown in Table 3.

## Discussion

Various indicators have been investigated as prognostic markers in patients with DLBCL. These include biological markers, clinical markers, and molecular markers detected using gene expression. In this study, we assessed the predictive role of LMR, RDW, and

**Table 3.** Multivariate analysis of prognostic factors of survival.

| Factors | OS | | | | PFS | | | |
|---|---|---|---|---|---|---|---|---|
| | Sig. | Hazard Ratio | 95% CI for Hazard Ratio | | Sig. | Hazard Ratio | 95% CI for Hazard Ratio | |
| | | | Lower | Upper | | | Lower | Upper |
| Age ≤60 years | | 1 | | | | 1 | | |
| Age >60 years | 0.865 | 0.923 | 0.364 | 2.338 | 0.190 | 0.506 | 0.183 | 1.403 |
| Male | | 1 | | | | 1 | | |
| Female | 0.517 | 1.236 | 0.652 | 2.343 | 0.137 | 1.700 | 0.845 | 3.421 |
| ECOG <2 | | 1 | | | | 1 | | |
| ECOG ≥2 | 0.092 | 1.920 | 0.899 | 4.102 | 0.297 | 1.515 | 0.694 | 3.308 |
| Stage I | | 1 | | | . | 1 | | |
| Stage II | 0.616 | 1.323 | 0.443 | 3.952 | 0.126 | 2.508 | 0.773 | 8.132 |
| Stage III | 0.170 | 2.536 | 0.671 | 9.587 | 0.190 | 2.463 | 0.640 | 9.473 |
| Stage IV | 0.024 | 6.556 | 1.283 | 33.513 | 0.032 | 5.355 | 1.160 | 24.718 |
| EN lesion ≤1 | | 1 | | | | 1 | | |
| EN lesion >1 | 0.043 | 0.306 | 0.097 | 0.964 | 0.039 | 0.273 | 0.080 | 0.936 |
| No B symptoms | | 1 | | | | 1 | | |
| B symptoms (yes) | 0.211 | 1.863 | 0.702 | 4.939 | 0.774 | 1.150 | 0.443 | 2.985 |
| R-IPI Poor | | 1 | | | | 1 | | |
| R-IPI Good | 0.757 | 0.816 | 0.226 | 2.949 | 0.005 | 0.140 | 0.036 | 0.546 |
| R-IPI Very good | 0.407 | 2.529 | 0.282 | 22.649 | 0.088 | 0.164 | 0.021 | 1.308 |
| LDH ≤250 | | 1 | | | | 1 | | |
| LDH >250 | 0.885 | 1.072 | 0.416 | 2.765 | 0.076 | 0.455 | 0.191 | 1.087 |
| B2MG ≤3 | | 1 | | | | 1 | | |
| B2MG >3 | 0.946 | .976 | 0.486 | 1.959 | 0.219 | 1.632 | 0.748 | 3.560 |
| Platelet <150 x$10^9$/dl | | 1 | | | | 1 | | |
| Platelet ≥150 x$10^9$/dl | 0.893 | 1.057 | 0.471 | 2.375 | 0.005 | 0.325 | 0.147 | 0.717 |
| High LMR (≥5.1) | | 1 | | | | 1 | | |
| Low LMR (<5.1) | 0.367 | 0.728 | 0.366 | 1.451 | 0.804 | 0.906 | 0.413 | 1.986 |
| Low RDW (<14.85) | | 1 | | | | 1 | | |
| High RDW (≥14.85) | 0.247 | 1.480 | 0.762 | 2.875 | 0.657 | 1.154 | 0.613 | 2.172 |
| Low NLR (<2.8) | | 1 | | | | 1 | | |
| High NLR (≥2.8) | 0.282 | 1.458 | 0.734 | 2.895 | 0.623 | 1.198 | 0.584 | 2.456 |

NLR values in the survival of DLBCL patients.

The CR rate in our study (61.7%) was slightly lower than universal data (3-5), however, the 5-year OS and PFS of (59.5% and 60% respectively) was concordant with international data among DLBCL patients treated with standard R-CHOP therapy (6, 7).

We found that many patients' characteristics like ECOG- PS ≥ 2, Ann Arbor stage IV, R-IPI of both poor and good category, having B symptoms and low platelet counts were associated with shorter 5-year PFS and OS. Moreover, multivariate analysis revealed that a shorter PFS also correlated with a high B2MG and more extranodal lesions (EN lesion >1). These findings are consistent with documented both IPI and R-IPI indices (7, 8, 10).

The evaluation of LMR can be used for diagnosis as a novel prognosticator in DLBCL patients (25). In the current study, LMR was significantly correlated with Ann Arbor staging only but did not correlate with other patients' characteristics like ECOG- PS, B symptoms, R-IPI, serum LDH, and B2MG. The LMR predicts the outcomes of PFS and OS in DLBCL patients who are treated with rituximab (26).

LMR was not correlated significantly with survival studies. In contrary with our findings, previous studies showed that patients with low LMR had a lower CR, and shorter PFS and OS (25-28); however, in line with our findings, Wang J *et al.,* Wei *et al*. and Yamauchi *et al*. stated that peripheral cell counts are not predictive for survival state in advance DLBCL patients (10). This contradiction probably related to different sample sizes, and using different cutoff values for LMR, and may conclude the restricted value of LMR as a single factor for predicting the prognosis in DLBCL; because the survival outcomes of patients are not only determined by the immune system but probably other factors like a genetic mutation, tumor size, the modality of treatment like chemotherapy or radiotherapy affect immune cell function and prognosis (29, 30). However, LMR did not possess value to predict OS and PFS, and it cannot be used as biomarkers for survival evaluation of DLBCL.

The RDW has emerged as a potential prognostic factor in malignancies. The results of a study showed that high RDW can be an adverse prognostic factor in patients with DLBCL who are treated with R-CHOP (31). RDW is performed commonly as part of a complete blood count (CBC) and plays a role in the diagnosis of anemia (32). RDW is a biomarker for breast tumors. Increased RDW pretreatment may be associated with a worse prognosis in women (33). In our study a high RDW was associated significantly with ECOG-PS ≥2, more frequent B symptoms, R-IPI of both poor and good score, and both high LDH and B2MG serum levels, these findings corresponded with other studies (1, 32). Furthermore, a high RDW was shown to associate with a lower 5-year OS and PFS, and a higher risk of death and relapse. Although the correlation between RDW and the survival study was not significant, it was matched with other studies (1, 21, 32). Accordingly, a high RDW at diagnosis could predict adverse prognosis in DLBCL patients. But RDW did not possess value to predict OS and PFS. Therefore, it cannot be used as biomarkers for survival evaluation of DLBCL.

The NLR is an independent prognostic factor for survival state in different types of malignancies, such as renal cell carcinoma, gastric cancer and colorectal cancer (34-36). It was identified that NLR was significantly associated with the level of LDH. Also, a high NLR was associated with a short OS and PFS. This finding was in agreement with other previous studies (37, 38). NLR has been known as a poor prognostic indicator in different solid tumors. The results of a study cannot detect the predictive value of NLR in patients with DLBCL (39). The results of another study demonstrated that NLR was correlated with poor OS and worse PFS (40). The results of our study showed that NLR did not possess value to predict OS and PFS, and cannot be used as biomarkers for survival evaluation of DLBCL. In this regard, a complete study of genes should also be considered. Because part of each phenotype is determined by genotype (41,42).

In this study the average age was younger than western data, 5-year OS and PFS were within standard international data, and the CR rate was lower. Low LMR was associated with more advanced Ann Arbor stage, while high RDW was associated significantly with ECOG- PS ≥2, more frequent B symptoms, R-IPI system of a poor and good score, and both high LDH and B2MG serum levels and NLR correlated with LDH level. The low LMR may predict lower PFS, while both high RDW and high NLR could predict a lower OS and PFS. As a result, LMR, RDW and NLR were correlated with many of patients' characteristics. However, none of the LMR, RDW and NLR did possess value to predict OS and PFS, and they cannot be used as biomarkers for survival evaluation of DLBCL.

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**Conflicts of interest**
The authors declare no conflicts of interest.

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