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Research Paper

The Overall Response Rate and Disease Free Survival in Patients with Diffuse Large B-cell Lymphoma Treated with Standard Therapy

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ABSTRACT:

BACKGROUND:

Diffuse large B-cell lymphoma (DLBCL) constitutes 30%–58% of non-Hodgkin's lymphomas. Treatment strategies should be stratified according to age, IPI and feasibility of dose-intensified approaches. Six cycles of combination chemotherapy (R-CHOP) is the current standard.

OBJECTIVE:

To assess the response rate and disease free survival in patients with Diffuse Large B- cell Lymphoma treated with standard therapy (R-CHOP).

PATIENTS AND METHODS:

An ambidirectional cross-sectional study with data obtained from November 2020 till December 2021 from Baghdad Teaching hospital / Department of Hematology. A total 100 adult patients who were diagnosed with diffuse large B cell lymphoma (DLBCL) and received R-CHOP were enrolled in this study.

RESULTS:

All the patients were evaluated using PET/CT or computed tomography scans with contrast (CeCT) post R-CHOP therapy: 53% patients were in complete response, 16% patients were in partial response, 20% patients were in progressive disease, 10% patients became primarily refractory to the therapeutic regimen. There was no significant association (P= 0.887) between the response to treatment and IPI scores. There was no significant association between patients' response to treatment and the prognostic factors of DLBCLs including age, LDH level, extra-nodal involvement and stage (P= 0.402, 0.281, 0.201, and 0.674 respectively).

CONCLUSION:

The current study showed that R-CHOP treatment has good response rate for patients with DLBCL with 53% of the patients were with complete response rate. Evaluation of patients by using PET/CT or CeCT after R-CHOP treatment showed that IPI score and patients' prognostic factors of DLBCLs including had no significant effect on achieving response.

KEYWORDS: Lymphoma, response rate, standard therapy.

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INTRODUCTION:

Diffuse large B-cell lymphoma (DLBCL) comprise heterogeneous group of aggressive malignancies of large, transformed B cell which cause diffuse effacement of the normal lymph node structure. The disease can arise de novo or may transform from an indolent lymphoma, such as small lymphocytic lymphoma or follicular lymphoma [(1)].

Diffuse large B-cell lymphoma (DLBCL) constitutes 30%–58% of non-Hodgkin's lymphomas. The crude incidence in Europe is 3.8/100 000/year [(2)]. The incidence increases with age and varies considerably across Europe. A family history of lymphoma, autoimmune disease, human immunodeficiency virus (HIV) infection, hepatitis C virus (HCV) infection, obesity as a young adult and some occupational exposures have been identified as risk factors of DLBCL [(3)]. In recent years, there have been important survival improvements for DLBCL [(4)].

The diagnosis of DLBCL should be carried out in a reference hematopathology laboratory with expertise in morphological interpretation and the facilities to carry out the full range of phenotypic and molecular investigations. A surgical excisional biopsy remains the optimal method of diagnosis. This allows assessment of nodal architecture and provides appropriate material for phenotypic and molecular studies. Ideally, the biopsy should be sent unfixed to the laboratory to allow flow cytometric studies to be carried out and high-quality DNA and RNA to be extracted [5].

The diagnosis of DLBCL should be confirmed in all cases by immunophenotypic investigations, or immunohistochemistry (IHC) or flow cytometry or a combination of both techniques [5].

The immunohistochemical study would include CD20, CD79a, BCL6, CD10, MYC, BCL2, Ki67, IRF4, CyclinD1, CD5 and CD23. EBER-1 staining may be used to identify the Epstein–Barr virus-positive DLBCL subtype of the elderly population. The report of histology should give the diagnosis according to the current World Health Organization classification [6].

Physical examination, performance status (PS) and history of B symptoms are important. A complete blood count, routine blood chemistry as well as screening tests for HIV, hepatitis B virus (HBV) and HCV are required. Positron emission tomography (FDG-PET)/computed tomography (CT) scan is now recommended as the gold standard for staging DLBCL patients [7,8]. PET/CT is more precise than contrast-enhanced CT (CeCT), with increased sensitivity for nodal and extranodal sites; in practice, CeCT is often carried out before PET/CT. a full diagnostic high resolution CT-scan should be carried out when necessary, in combination with PET/CT [9].

Despite developements in the treatment of DLBCL, the outcome of patients with DLBCL remains variable. Although potentially curable, about 40% of patients will die with relapsed or refractory disease. A number of clinical and biological prognostic or predictive markers have been described. The International Prognostic Index (IPI) was devised in 1993 and remains the most widely used prognostic tool [10] The IPI is useful clinically because it is reproducible, allows accurate scoring and categorizes patients. Several modified versions of IPI according to the subtypes of NHL have been described [11].

Six cycles of combination chemotherapy with cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP) treatment combined with six doses of rituximab given every 21 days is the current standard [12].

MATERIALS AND METHODS:

This is ambidirectional cross-sectional study with data obtained from November 2020 till December 2021 from Medical city complex / Baghdad Teaching hospital / Department of Hematology.

A total 100 adult patients who were diagnosed with diffuse large B cell lymphoma (DLBCL) and received R-CHOP were enrolled in this study after appliance of the inclusion and exclusion criteria. All patients were informed about the study and consent taken. All patients received the protocol that includes rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone (R-CHOP) chemotherapy.

Inclusion criteria:

- Patients aged 1٥ years and above.
- A biopsy proved DLBCL reviewed by two histopathologists.

Exclusion criteria:

- Patients with missed initial investigations.
- Patients with loss follow up.
- Patient received chemotherapy other than R-CHOP /21 days.

RESULTS:

We evaluated a totally collected of 100 adult patients were diagnosed with diffuse large B cell lymphomas (DLBCLs) and they are treated with standard chemo-immunotherapy (R-CHOP). Patients' age ranged from 15 to 70 years with a mean of 44.72 years and standard deviation (SD) of ± 13.86 years, and 46 patients were found in the age group of (45 - 60) years. There were 58 males versus 42 females, with a male to female ratio of 1.38:1.

Patients' characteristics are listed in Table (3.2), 52% of patients were in advanced stages while the remaining 48% were in early stage, Concerning factors of IPI, 16% of patients aged > 60 years, 18% of patients had serum LDH levels higher than normal, 20% had ≥ 2 extra-nodal disease site, and 52% of patients were with Ann Arbor stage III or IV. IPI scores for the study patients were as follows: 72% of patients were low-risk, 21% were low-intermediate-risk, 6% were high-intermediate-risk, and 1% was high-risk. (Table 1).

Table 1: Baseline patients Characteristics of Diffuse Large B-Cell Lymphoma.

Clinical Characteristics	No. (n= 100)	Percentage (%)
Stage		
Early	48	48.0
Advanced	52	52.0
Negative Prognostic Factors		
Age > 60 Years	16	16.0
Elevated LDH	18	18.0
Extranodal Site ≥ 2	20	20.0
Performance Score ≥ 2	0	0
Ann Arbor Stage III or IV	52	52.0
IPI Scores*		
Low Risk	72	72.0
Low- Intermediate Risk	21	21.0
High- Intermediate Risk	6	6.0
High Risk	1	1.0

All of the patients were evaluated using PET/CT or computed tomography (CT) scans with contrast post R-CHOP therapy were notable as follows: 53% of patients were in complete response, 16% of patients were in partial response, 20% of patients were in progressive disease, 10% of patients became primarily refractory to the therapeutic regimen, while one patient didn't receive therapy. In this study, there was no significant association between patients' response to treatment and the prognostic factors of DLBCLs including age, LDH level, extranodal involvement, and Ann Arbor stage (Table 2).

Table 2: The association between response to treatment and different prognostic factors of DLBCLs.

Prognostic Factors	Response to Treatment				P- Value
	CR (%) n= 53	Partial (%) n= 16	Refractory (%) n= 10	Progressive Disease (%) n= 20	
Age > 60 Years					
Yes (16)	11/16 (68.8)	2/16 (12.5)	0/16 (0)	3/16 (18.7)	0.402
No (84)	42/84 (50.6)	14/84 (16.9)	10/84 (12.0)	17/84 (20.5)	
Elevated LDH					
Yes (18)	12/18 (66.7)	4/18 (22.2)	1/18 (5.6)	1/18 (5.6)	0.281
No (82)	41/82 (50.6)	12/82 (14.8)	9/82 (11.1)	19/82 (23.5)	
Extranodal site ≥ 2					
Yes (20)	15/20 (75.0)	2/20 (10.0)	1/20 (5.0)	2/20 (10.0)	0.201
No (80)	38/80 (48.1)	14/80 (17.7)	9/80 (11.4)	18/80 (22.8)	
Ann Arbor Stage III or IV					
Yes (52)	29/52 (55.8)	9/52 (17.3)	6/52 (11.5)	8/52 (15.4)	0.674
No (48)	24/48 (51.1)	7/48 (14.9)	4/48 (8.5)	12/48 (25.5)	

DISCUSSION:

Large B-cell lymphomas, represent almost 30% of all cases of non-Hodgkin's lymphoma. Patients typically present with progressive extra nodal disease, lymphadenopathy, or both and require therapy [13].

This study involved 100 patients with age ranged from 15 to 70 years with a mean of 44.72 years, about half of patients were in the age group of (45 - 60) years, and were males (male to female ratio of 1.38:1) This is still younger age group than what had been shown in a retrospective study that conducted in Shorsh General Hospital/ Sulaimani on 61 patients with confirmed diagnosis of DLBCL. The mean age at diagnosis was about 51 years with peak age of incidence between 50 and 64 years with female predominance [14].

The current study revealed that more than half of patients were in advanced stages and this is comparable with Sehn LH et al in 2021 [15].

This study found that 72% of patients were of low-risk, 21% were low-intermediate-risk, 6 % were of high-intermediate-risk, and only one patient was of high-risk. These finding were based on the factors of IPI classification, while in Changhoon Yoo et.al in 2010, patients were of low, intermediate and high risk were 12.7%, 54.3% and 12% respectively [16].In the present study, 53 patients were in complete response after R-CHOP therapy, 16 patients were in partial response, 20 patients were in progressive disease, 10 patients became primarily refractory to the therapeutic regimen, and only one patient didn't receive therapy and this is incomparable with Vose JM in 2005 who studied Thirty-three patients with untreated aggressive B-cell lymphoma and received six infusions of rituximab given on day 3 of each cycle of therapy. The overall response rate was 94% while the complete response rate was 61% in those patients at the end of therapy [17].

CONCLUSION:

1. R-CHOP regimen considered as an effective protocol whereas, total response rate to treatment with R-CHOP in 69% including complete response rate in 53% and partial response rate in 16% which is considered a good rate, and 20% of patients had a progressive disease and 10% of patients had refractory disease.
2. There was no significant association between the patients' response rate to R-CHOP treatment and their IPI score.
3. There was no significant association between patients' response rate to R-CHOP treatment with age, LDH level, extra-nodal involvement, and Ann Arbor stage.

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