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# Evaluation Of Treatment Response According To Clinical Prognostic Factors Of Diffuse Large B Cell Non-Hodgkin Lymphoma

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ORIGINAL ARTICLE

# Evaluation of Treatment Response According to Clinical Prognostic Factors of Diffuse Large B Cell Non-Hodgkin Lymphoma

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**Abstract**

*Background*: **Non-Hodgkin lymphomas (NHL) are heterogeneous neoplasms of the lymphoid tissues variously derived from B cell, T cell, natural killer cell. In Egypt, NHL represent 4.64 % of all cancer. NHL is the fifth most frequent malignancy.**

*Aim and objectives*: **To evaluate the Treatment Response According to Clinical Prognostic Factors Of Diffuse Large B Cell Non-Hodgkin Lymphoma.**

*Subjects and methods*: **This study was a retrospective analysis of sixty individuals diagnosed with diffuse large B cell non-Hodgkin's lymphoma (DLBCL) and treated at El Hussein hospital's Clinical Oncology Department, Faculty of Medicine El Azhar University throughout the period among January 2015 to October 2022.**

*Result*: **About 81.7 % of study was more than 60 years the majority of patients were male patients. The commonest site of extra-nodal involvement was spleen patients followed by BM patients. The most common presenting symptoms was painless swelling in patients. As regards mortality rate distribution, it found that (31.7 %) 19/60 patients died and (68.3 %) 41/60 patients were alive and disease free on last visit. There was a difference that may be considered statistically significant among the studied groups regarding OS among DLBCL cases who received CHOP regimen according to PS subgroups.**

*Conclusion*: **The current study showed that the dosage intensity of cyclophosphamide and doxorubicin will play an essential role in the treatment regimen plan for DLBCL in the future, particularly in patients at greater risk. Complete response (CR) was higher in males who had normal LDH, had good PS, presented with early stages and lower IPI risk, the intensity of the dosage of doxorubicin and cyclophosphamide had a substantial impact on the CR rate.**

*Keywords:* Diffuse large B cell, Mabthera, Non-Hodgkin lymphoma, Toxicity

## 1. Introduction

Different types of B cells, T cells, and natural killer cells can give rise to NHL, making this kind of lymphoma extremely diverse. 4.64 % of all cancer cases in Egypt are caused by NHL. When it comes to cancers, NHL ranks in at number five.[1]

Forty% of all lymphoid malignancies are diagnosed as DLBCL, making it the most frequent form of B cell lymphoma. The rapid clinical course and clinical, pathological and molecular heterogeneity that define LBCL also make it challenging to decide on a treatment and predict the disease's prognosis.[2]

Germinal center B cell (GCB) and activated B cell (ABC) are the two most common molecular subtypes of DLBCL, each with their own unique biology. When contrasted with those suffering from non-ABC DLBCL, those who undergo conventional chemoimmunotherapy had much worse results. Besides the GCB and ABC subtypes, double-hit

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lymphomas (affecting around 5–10 % of cases) are also aggressive DLBCLs with a dismal prognosis because they overexpress MYC and BCL2 protein.[3]

In over half of patients, standard treatment for diffuse large cell lymphoma is effective in curing the disease. Many others, nevertheless, suffer from malignancies that are resistant to standard treatments or that return following an initial response to treatment.[4]

Rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone administered over the course of six cycles (R–CHOP) is the present gold standard for treating DLBCL. Drugs including methotrexate, bleomycin, and cytarabine have been used in subsequent innovative combinations, but randomized multi-center trials have failed to show that these treatments improve survival rates over the gold-standard CHOP.[5]

The prognosis is dismal, especially with high-dose salvage regimens, for cases with aggressive NHL who do not react well to first-line therapy or who relapse quickly. Recently, it has been common practice to keep the RDI of chemotherapeutic medicines at a higher level in an effort to improve results in the treatment of aggressive lymphoma. It is important to identify patients who have early treatment failure on first-line therapy so that they can begin a more intense regimen without delay.[6]

The study set out to: Our primary goal was to assess the clinical prognostic variables that influence the consequence and prognosis of our DLBCL cases who were treated with the first-line CHOP regimen with or without mabthera, and to assess the responsiveness to therapy based on these parameters. As a secondary goal, we looked at treatment-related toxicity, progression-free survival, and overall survival (OS) across every one of the subgroups.

## 2. Patients and methods

This research was a retrospective analysis of sixty individuals diagnosed with DLBCL and treated at El Hussein hospital's Clinical Oncology Department, Faculty of Medicine El Azhar University throughout the duration among January 2015 to October 2022. Data of patients were collected from files of patients in the archive department.

### 2.1. Inclusion criteria

Histopathologically proven of DLBCL, Patients received and finished treatment at our department, Age between (18) and (80) years old, Performance status (0 to III) WHO and Follow-up at least 6 months.

### 2.2. Exclusion criteria

Primary Cns NHL involvement at presentation, HIV positive patients and Associated malignant tumor instead of NHL.

All cases data were collected in an excel sheet for all patients: Age more than 18 years, Both sex, Comorbid conditions (DM,HTN,CARDIAC …), Clinical presentation (Abdominal pain, Enlarged swelling), Constitutional manifestation as night fever, sweating, loss of appetite and unexplained Wight loss, Date of diagnosis, Duration between symptoms and definitive treatment, Date of progression, Date of last contact and status of the patient at that date, LDH normal (<420) or above normal, bulky disease below or above 5 cm and Extra-nodal involvement (spleen, gastric. BM …).

### 2.3. Treatment plan

Patients were going to receive the usual CHOP chemotherapy regimen, which consists of cyclophosphamide 750 mg/m$^2$ on day one of treatment, doxorubicin 50 mg/m$^2$ on day one of treatment, vincristine 1.4 mg/m$^2$ on day one of treatment, and prednisone 100 mg PO for five days. The initial chemotherapy treatment was going to consist of 3 or more cycles in a row. Reviewing the cases' medical records allowed for the collection of clinical data as well as information regarding follow-up.

Response rate was classified as CR, PR, SD OR DP along with the standardized international workshop criteria.[6]

Complete Response (CR) is the removal of all signs and symptoms of an illness that was previously present. The term 'Partial Response' (PR) refers to a reduction of 50 % in the sum of the products of the biggest perpendicular diameter of the masses that were already present. Progressive disease (PD) is defined as a rise of 25 % in the size of the products of the biggest perpendicular diameters of the pre-existing masses. On the other hand, stationary disease (SD) is regarded in any other situation.

### 2.4. Statistical analysis

The statistical analysis of OS and disease-free survival will be performed using the one-sided log-rank test of Kaplan-Meier survival estimation. The unpaired T test and the one-way ANOVA test test will be utilized for the univariate analysis of the variables.

## 3. Results

Table 1.

*Table 1. Demographic characteristics amongst the studied cases.*

| | Patients ($n$ = 60) |
|---|---|
| **Age** (years) | |
| Mean ± SD | 45.13 ± 12.73 |
| Median (range) | 47.5 (20–67) |
| **<60 years** | 49 (81.7 %) |
| **[3]60 years** | 11 (18.3 %) |
| **Total** | 60 (100 %) |
| **Sex** | |
| Female | 22 (36.7 %) |
| Male | 38 (63.3 %) |
| Ratio Male: female | 1.7:1 |
| **Total** | 60 (100 %) |

The median age was 47.5 years (range; 20–67 years) and about 81.7 % of study was more than 60 years the majority of patients weremale (63.3 %) 8/60 patients, while (36.7 %) were female (22/60) patients. The male to female ratio 1.7:1 Figs. 1 and 2, Table 2.

AS regard to site of extra-nodal involvement the commonest site of extra-nodal involvement was spleen (16.7 %) 10/60 patients followed by BM (15 %) 9/60 patients, gastric (10 %) 6/60 patients then nasopharynx (5 %) 3/60 patients Table 3.

The most common presenting symptoms was painless swelling in (63.3 %) 38/60 patients while Symptoms due to obstruction by enlarged lymphoid tissue including dysphagia, dyspnea, nasal obstruction were complaint in (20 %) 12/60 patients However, general symptoms including fever, loss of weight, night sweeting, fatigue, pain were encountered in (58.3 %) 35/60 patients Fig. 3, Table 4.

As regards mortality rate distribution, it found that (31.7 %) 19/60 patients died and (68.3 %) 41/60 patients were alive and disease free on last visit.

The strength of the dosage of doxorubicin and cyclophosphamide has a considerable impact on the

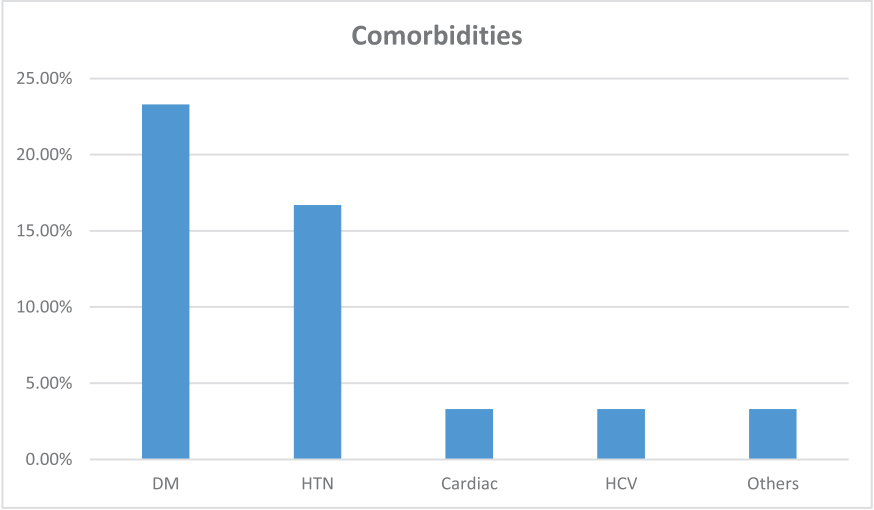


*Fig. 1. Comorbidities distribution among the studied patients.*

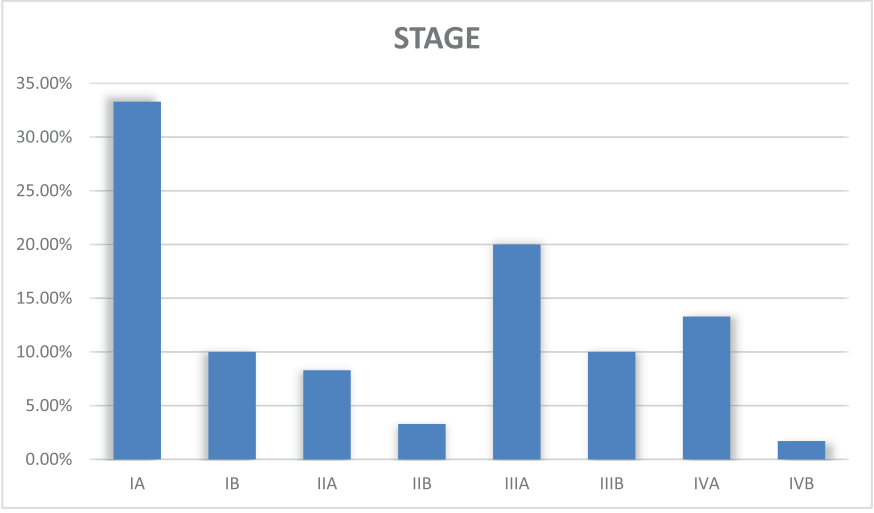


*Fig. 2. Stage distribution among the studied patients.*

*Table 2. Site of extra-nodal involvement among the studied patients.*

| | *N* (%) |
|---|---|
| Abdominal Mass | 1 (1.7) |
| BM/Liver/Spleen/lung | 9 (15 %) |
| Breast | 1 (1.7) |
| Colon | 1 (1.7) |
| Colon/Ovary | 1 (1.7) |
| Duodenal | 1 (1.7) |
| Elbow Mass | 1 (1.7) |
| Gastric | 6 (10) |
| Gastric/Pancreatic | 1 (1.7) |
| Intrascapular lesion | 1 (1.7) |
| Larynx | 1 (1.7) |
| Maxilla | 1 (1.7) |
| Nasopharynx | 3 (5) |
| Oropharyngeal Mass | 1 (1.7) |
| Ovary | 1 (1.7) |
| Parapharyngeal Mass | 1 (1.7) |
| Parotid | 1 (1.7) |
| Spleen | 10 (16.7) |
| Spleen/Vertebral Mass | 1 (1.7) |

*Table 3. Clinical presentation distribution among the studied patients.*

| | *N* (%) |
|---|---|
| Swelling | |
| Yes | 38 (63.3) |
| No | 22 (36.7) |
| Total | 60 (100 %) |
| General symptoms | |
| Yes | 35 (58.3) |
| No | 25 (41.7) |
| Total | 60 (100 %) |
| Obstructive symptoms | |
| Yes | 12 (20 %)) |
| No | 48 (80 % |
| Total | 60 (100 %) |

CR rate. The CR rate was 80.4 % 37/46 cases when the doxorubicin DI was below or equal to the median (16.5 mg/m$^2$/week), but it was 19.6 % 9/46 cases when the doxorubicin DI was over the median. When the relative dosage intensity of doxorubicin was at or below the median, the CR rate was 80.4 % 37/46 cases (Table 5), while it was only 19.4 % (9/46 patients) when the RDI was over the median. The CR rate for cyclophosphamide dose intensities (DI) below or equal to the median (250 mg/m2/week) was 71.7 % for 33 out of 46 cases, whereas the CR rate for DIs over the median was 28.3 % for 13 out of 46 cases. With an RDI that was either below or equal to the median, the CR rate was 71.7 % 33/46 cases, but the CR rate was only 27.7 % 13/46 cases when the RDI was over the median Table 6.

This table demonstrated that there was a statistically significant difference among the groups that were evaluated in terms of OS among DLBCL patients who underwent the CHOP regimen based on PS subgroups.

## 4. Discussion

Due to the aggressive nature of DLBCL, many patients present with advanced illness. The International Prognostic Index (IPI) is a tool used to estimate the prognosis of cases with DLBCL. Disease stage, number of extra-nodal disease sites, age, and blood lactate dehydrogenase level all factor into the IPI score. The Eastern Cooperative Oncology Group performance status also plays a role.[7]

### *4.1. The main results of this study were as follows*

Regarding demographic data, it was revealed that the median age was 47.5 years (range; 20–67 years) and males 63.3 % to females 36.7 (1.7:1). Regarding comorbidities the most prevalent comorbidity was DM (23.3 %), HTN (16.7 %), HCV 3.3 % and cardiac 3.3 %, while there were 68.4 % of the patients were free. About 30 % of study group are smoker, 1.6 % were alcoholic and 5 % drug addicted.

Comparable with the current study Bardakci et al.[8] enrolled 91 patients with DLBCL, and revealed that the median age of 58 (20–81, minimum–maximum) years, with predominance of males (64.8 %). Also, Gogia et al.[9] enrolled 267 patients with DLBCL, and revealed that the median age was 49 (20–81) years with male: female ratio of 2:1. The current study revealed that ECOG performance status 1 was the commonest (83.3 %) whereas, PS 2 (10 %) PS 0 were (5 %) and PS 3 were (1.7 %). In concordance with Bardakci et al.[8] who revealed that the most common ECOG was PS 1 in (66 %) in DLBCL patients. Also, Gogia et al.[9] showed that PS 1 was the most common among (41 %) followed by PS 2 in (20 %). As well, Abdelhamid et al.[10] in an Egyptian study of 224 DLBCL patients showed that the most common ECOG was PS 1 in (71 %) followed by PS 2 in (25.9 %). In the present research, it was found that 55 % of the cases had elevated lactate dehydrogenase (LDH), 72 % of the patients had extra-nodal involvement and majority of them had one extra-nodal involvement (63.3 %). 51.7 % of the patients presented with B symptoms with mean duration from symptoms to diagnosis was 2.81 ± 2.19 months.

However, Abdelhamid et al.[10] revealed that The LDH levels of 71 % of the cases were elevated. For a total of 93 cases, 41.5 % had involvement outside of the lymph nodes. B symptoms was present in (29.5 %).

According to the presenting symptoms, the most prevalent presenting symptoms was abdominal Pain (33.3 %) followed by neck swelling (13.3 %), axillary LN (10 %) then inguinal swelling (5 %).

Consistent with Bardakci et al.[8] who revealed that the most common symptoms were abdominal pain

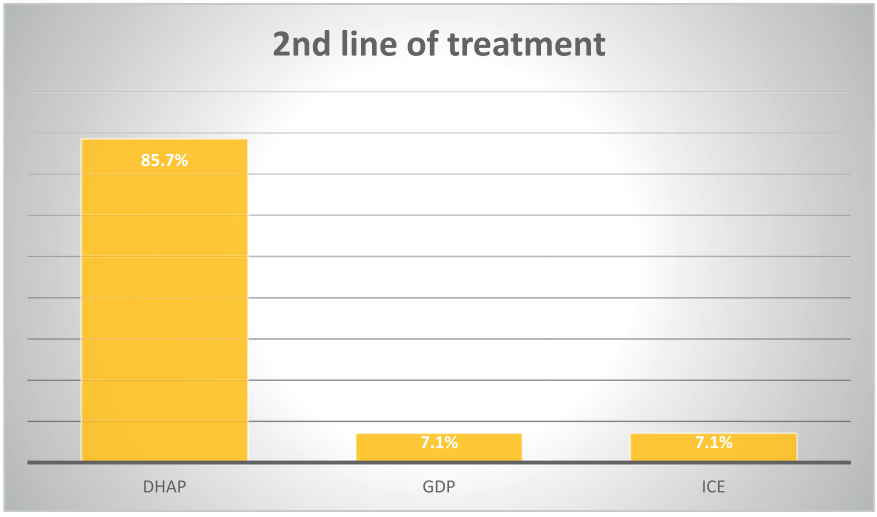


*Fig. 3. Second line treatment among the studied patients.*

*Table 4. Mortality rate distribution among the studied patients.*

| | Patients ($n$ = 60) $N$ (%) |
|---|---|
| Alive | 41 (68.3 %) |
| Dead | 19 (31.7 %) |
| Total | 60 (100 %) |

*Table 6. OS among cases with DLBCL who were treated with the CHOP treatment, classified by PS subgroups.*

| PS | Mean | S.E. | 95 % Confidence Interval | Log rank$^{MC}$ | $P$ |
|---|---|---|---|---|---|
| 0–1 | 66.777 | 4.583 | 57.795–75.760 | 40.886 | **<0.001** |
| 2–3 | 13.571 | 2.493 | 8.686–18.457 | | |

(54.9 %) and dyspepsia (17.6 %). Consistent with the findings of the present investigation MAHBUB et al.[11] revealed that the most common symptoms were pain (54.2 %) and swelling (24.9 %). It was found that most of the patients had IPI of 1 and 2 (43.3 %, 33.3 %). While that most of the patients had age adjusted IPI of 1 (41.7 %). However, Bardakci et al.[8] showed that the number of cases with an International Prognostic Index (IPI) score of 0–2 (low–low-intermediate risk) was 54 (59.4 %), the number of cases with an IPI score of 3 (high intermediate) was 19 (20.9 %), and the number of patients with an IPI score of 4–5 (high-risk) was 18 (19.8 %). Also, Gogia et al.[9] corresponding to the international prognostic index (IPI), the distribution was as follows: 40 % had a low risk, 45 % had an intermediate risk, and 15 % had a great risk.

In addition, Babu et al.[12] demonstrated that the percentage of patients who presented in low, low-intermediate, high-intermediate, and high-risk categories on the International Prognostic Index (IPI) was 148 (28.13 %), 191 (36.31 %), 124 (23.57 %, and 63 (11.97 %), respectively.

*Table 5. Correlation of dose intensity and relative dose intensity with CR among the studied patients.*

| | CR ($n$ = 46) $N$ (%) | No CR ($n$ = 14) | | |
|---|---|---|---|---|
| Dose intensity of Doxorubicin | | | | |
| Below or equal median (16.6 mg/m$^2$/week) | 37 (80.4 %) | 12 | 85.7 % | 0.013 |
| Above median | 9 (19.6 %) | 2 | 14.2 % | |
| Total | 46 (100 %) | 14 | 100 % | |
| Relative dose intensity of Doxorubicin | | | | |
| Below or equal median | 37 (80.4 %) | 12 | 85.7 % | 0.013 |
| Above median | 9 (19.6 %) | 2 | 14.2 % | |
| Total | 46 | 14 | | |
| Dose intensity of Cyclophosphamide | | | | |
| Below or equal median (250 mg/m$^2$/week) | 33 (71.7 %) | 11 | 78.5 % | 0.008 |
| Above median | 13 (28.3 %) | 3 | 21.5 % | |
| Total | 46 | 14 | | |
| Relative dose intensity of Cyclophosphamide | | | | |
| Below or equal median | 33 (71.7 %) | 11 | 78.5 % | 0.008 |
| Above median | 13 (28.3 %) | 3 | 21.5 % | |

This is in accordance with the findings of Abdelhamid et al.,[10] who found that all cases were given the first CHOP regimen with a number of cycles ranging from three to eight cycles, with six cycles serving as the median. Complete remission (CR) was obtained in 178 out of 224 cases (79.5 %), whereas no CR (PR, SD, or PD) was observed in 46 out of 224 cases (20.5 %). At a median observation period of 12 months, recurrence was detected in 27 out of 178 cases who had achieved full remission. This is a 15.2 % incidence rate.

As regards mortality rate distribution, it found that 31.7 % of the patients died and 68.3 % were alive and disease free on last visit. Comparable with LASSALLE et al.[13] who revealed that here were 40 (27.0 %) deaths of which 23 (57.5 %) died of lymphoma progression without other comorbidities, 15 (37.5 %) died of infectious diseases. However, MAHBUB et al.[11] showed that the death rate was 16.6 %. While Gogia et al.[9] showed that the mortality rate was 11.2%To assess the factors associated with CR, we performed a comparison between patients with and without CR, it was revealed that compared to patients who did not achieved CR, patients who achieved CR after first-line Ctx were significantly more prevalent in males, had normal LDH, had good PS, presented with early stages of the disease and lower IPI risk.

Consonant the current study Abdelhamid et al.[10] revealed that the CR rate was significantly influenced by PS, stage, LDH level and IPI, as patients who achieved CR were significantly had normal LDH, had good PS, presented with early stages of the disease and lower IPI risk.

This comes in agreement with Abdelhamid et al.[10] who revealed that the CR rate is significantly influenced by the dose intensity of Doxorubicin and Cyclophosphamide. With Doxorubicin DI £(16.5 mg/m2/week), the CR rate.

Multivariate regression analysis of factors associated with mortality among DLBCL cases who received CHOP regimen, showed that, higher stage (III and IV) and bulky tumor (>5 cm) were significantly associated with higher mortality rate among DLBCL patients who received CHOP regimen.

In agreement with the current study Abdelhamid et al.[10] revealed that bulky tumor (>5 cm) was significantly associated with higher mortality rate among DLBCL cases who received CHOP regimen. But in contrast to the current study, they revealed that stage was not shown to be a significant independent predictive factor in relation to OS, the disagreement may be due to the difference in sample size and stage distribution. Also, in concordance with the current study Bardakci et al.[8] showed that advanced stage was significantly associated with higher mortality rate among DLBCL patients regardless of treatment regime, in Univariate analysis.

The current study showed that the median disease-free survival (DFS) following first-line CTx (DFS) was 57.75 months (95 % confidence interval 48.1–67.34 months). However, Abdelhamid et al.[10] revealed that the DFS ranged from 1 to 45 months with a 2-year DFS of 68.8 %.

Also, MAHBUB et al.[11] showed that the 5-year OS and DFS rates were 66.7 % and 77.8 %, respectively in a Kaplan-Meier analysis. The current study showed that the mean OS time was 60.8 months (95 % confidence interval 51.65–70.02 months). OS was significantly longer in cases with early disease stages and lower-risk IPI scores.

### *4.2. Conclusion*

According to the findings of this study, the dosage intensity of cyclophosphamide and doxorubicin should play a significant role in the development of the future treatment regimen plan for DLBCL, particularly in high-risk patients. CR was greater in men who had normal LDH, had excellent PS, presented with early stages, and had a decreased IPI risk. The dosage intensity of doxorubicin and cyclophosphamide had a significant impact on the CR rate. Earlier stage, less than 2 extra-nodal involvement, lower IPI were independent predictors of CR. More advanced stage and Bulky tumor (>5 cm) were associated with mortality among DLBCL cases who received CHOP regimen. OS and DFS were significantly affected by age, stage, IPI group, PS, LDH level, the presence of B-symptoms and Dose intensity of Cyclophosphamide.

## Disclosure

The authors have no financial interest to declare in relation to the content of this article.

## Authorship

All authors have a substantial contribution to the article.

### Conflicts of interest

The authors declared that there were NO conflicts of Interest.

## References


1. Ibrahim AS, Khaled HM, Mikhail NN, Baraka H, Kamel H. Cancer incidence in Egypt: results of the national population-based cancer registry program. *J Cancer Epidemiol*. 2014;2014.
2. Rosenwald A, et al. The use of molecular profiling to predict survival after chemotherapy for diffuse large-B-cell lymphoma. *N Engl J Med*. 2002;346:1937–1947.
3. Nowakowski GS, Czuczman MS. ABC, GCB, and double-hit diffuse large B-cell lymphoma: does subtype make a difference in therapy selection? *Am Soc Clin Oncol Educ Book*. 2015; 35:e449–e457.
4. Chavez JC, Bachmeier C, Kharfan-Dabaja MA. CAR T-cell therapy for B-cell lymphomas: clinical trial results of available products. *Ther Adv Hematol*. 2019;10:2040620719841581.
5. Vitolo U. A randomized multicentre phase III study for first line treatment of young patients with high risk (AAIPI 2-3) diffuse large B-cell lymphoma (DLBCL): rituximab(! R) Plus dose-dense chemotherapy CHOP14/MEGACHOP14 with or without intensified high-dose chemotherapy (HDC) and autologous stem cell transplantation (ASCT). results of DLCL04 trial of Italian Lymphoma Foundation (FIL). *Ann Oncol*. 2011;22:iv106.
6. Cheson BD, et al. Revised response criteria for malignant lymphoma. *J Clin Oncol*. 2007;25:579–586.
7. Abdelhamid T, Samra M, Ramadan H, Mehessin M, Mokhtar N. Diffuse large B-cell lymphoma: 10 years' real-world clinical experience with rituximab plus cyclophosphamide, doxorubicin, vincristine and prednisolone. *Oncol Lett*. 2018;15:3602–3609.
8. Babu SM, Garg S, Kanakasetty GB, Kuntegowdanahalli LC, Dasappa L, Rao SA., et al. Evaluation of clinical and prognostic factors for primary gastric diffuse large B-cell lymphoma: single-center experience. *J Cancer Res Therapeut*. 2023; 8:60.
9. Gogia A, et al. Diffuse large B-cell lymphoma: an institutional analysis. *South Asian J Cancer*. 2018;7:200–202.
10. Abdelhamid T, et al. Clinical prognostic factors of diffuse large B cell non-Hodgkin lymphoma: a retrospective study. *J Egypt Natl Cancer Inst*. 2011;23:17–24.
11. Mahbub AAH. *The Anti-cancer Potential of Polyphenols in the Treatment of Leukaemia*. Sheffield Hallam University (United Kingdom); 2015.
12. Babu SMC, et al. Diffuse large B-cell lymphoma: a retrospective study from a regional care center in South India. *Indian J Cancer*. 2018;55:66–69.
13. Larouche JF, Berger F, CJzassagne-Ciement C, et al. Lymphoma recurrence 5 years or later is following diffuse large B-cell lymphoma: clinical characteristics and outcome. *J Clin Oncol*. 2010;28:2094.