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Research Article

The Cell of Origin of Diffuse Large B-cell Lymphoma: Is It a Predictor for Response Rate?

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ABSTRACT

Background: Diffuse large B-cell lymphomas not otherwise specified (DLBCL-NOS), is the most common lymphoma subtype, which is further divided into germinal center B-cell (GBC), activated B-cell (ABC), and unclassifiable. In Iraq, 1,010 deaths due to non-Hodgkin lymphoma were reported in 2020.

Aim of the study: This study aims to assess the role of cell of origin (COO) of diffuse large B-cell lymphoma as a predictor of response to frontline treatment.

Subjects and Methods: A cohort study was conducted on cases of Diffuse DLBCL-NOS at the Baghdad National Center of Hematology at Baghdad Teaching Hospital, Medical City, Bagdad from1st January 2021 to 1st September 2022. All cases received same treatment, and treatment response was assessed at interim and end of treatment using Lugano classification.

Results: The study included 134 cases of DLBCL-NOS, of which 18.7% were GCB and 81.3% were ABC type. GCB cases had higher rates of early-stage disease and lower International Prognostic Index risk than ABC cases. The rate of complete response was higher in GCB cases than ABC cases. Partial response or progressive disease were associated with ABC cases but on further analysis we found that the International Prognostic Index (IPI) score was the only predictor of complete response, and Lactate dehydrogenase level was the only predictor of overall survival. COO did not affect progression-free survival or overall survival.

Conclusions: COO had no effect on response to treatment and had no survival benefits while IPI score was found to be a good predicter of complete response and survival.

Introduction

Lymphomas are neoplasms arising from lymphoid tissues and are diagnosed from the pathological findings on biopsy. The majority are of B-cell origin. Non-Hodgkin lymphomas (NHL) are classified as low- or high-grade tumors based on their proliferation rate (1). Annually, more than 150,000 new cases of Large B-cell lymphomas diagnosed over the globe, which represents almost 30% of all cases of NHL (2). In Iraq, according to world health organization-international agency for research on cancer, the total number of cases of NHL diagnosed from 2015-2020 was 4,528 cases, with an estimated prevalence 11.3 per 100,000 population. NHL ranked 6th most lethal cancer in Iraq (3).

In 2000, Alizadeh and colleagues utilized gene expression profiling (GEP) to analyze 96 normal and DLBCL cells. They identified three distinct genetic signatures that corresponded to three different

subtypes of the disease, based on cell of origin (COO). These included the germinal centre B-cell (GCB)-like subtype, which is similar to the GEP of normal GCBs, the activated B-cell (ABC)-like subtype, which is similar to normal ABCs, and an unclassifiable condition in the remaining 10%-15% of samples. Despite initially being found by GEP, that analysis has not been widely used in clinical practice due to its high cost and the requirement for fresh frozen tissue. In clinical practice, immunohistochemistry (IHC) algorithms, such as the Hans and Tally methods, are employed to determine COO, but their agreement with GEP might vary (4).

Several studies have demonstrated that patients with the ABC disease subtype experience considerably worse results when treated with typical upfront rituximab-containing combination therapy compared to those with GCB illness. The prognostic impact of COO in relapsed illness is yet uncertain. The Bio-CORAL trial indicated that patients with GCB DLBCL who received R-DHAP treatment had a higher 3-year progression-free survival (PFS) rate compared to those who received R-ICE treatment (5). Er aimed in this study to define the role of COO of diffuse large B-cell lymphoma as a predictor of response to frontline treatment

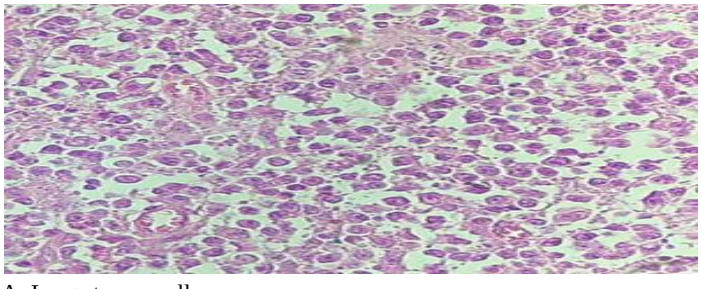
Subjects and Methods

The present study was conducted at the Baghdad National Center of Hematology at Baghdad Teaching Hospital, Medical City, Baghdad during a period from 1st January 2021 to 1st September 2022. The study included all adult cases of DLBCL not otherwise specified diagnosed. Other subtypes of large B cell lymphoma, low grade lymphoma transformed to DLBCL, patients lost from follow up, and treatment other than R-CHOP were excluded.

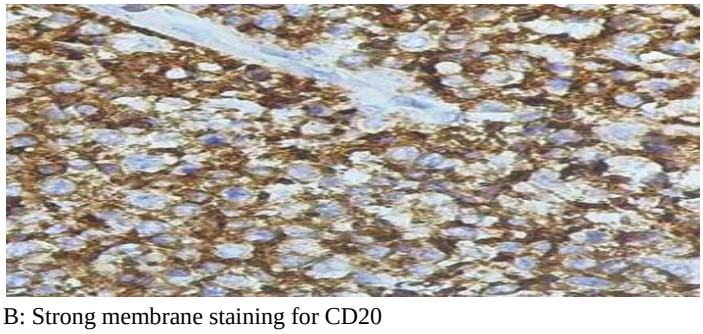
A questionnaire was designed to collect the following data: patient age, past medical, surgical, and drug histories, symptoms at presentation (B symptoms, lymphadenopathy, organomegaly, bleeding tendency, and mediastinal mass), and determination of eastern cooperative oncology group (ECOG) score. Blood investigations were done including: complete blood count, serum albumin, blood urea, serum creatinine, serum lactate dehydrogenase (LDH), erythrocyte sedimentation rate, and serum uric acid. All biochemical tests were performed by Automated analyzer (Architect plus c4000, cobas c 311) at Baghdad Teaching Hospital. Imaging studies (either CT or PET-CT) for the staging, estimation of the number of the involved extra nodal sites were also done as well as application of Ann Arbor staging system. All cases had undergone bone marrow aspirate and biopsy. The biopsy sample was sent for histopathological study requesting both morphology and immunohistochemistry. All the patients received R-CHOP (i.e., rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) (6) immunochemotherapy according to the stage (stage I, and IIA received three to four cycles with or without radiotherapy while stage IIB, III, and IV received six cycles.

The assessment of the treatment response was done at interim and end of treatment. The response assessment included CT/PET-CT Lugano classification into four groups: complete, partial, stable, and progressive, according to the reduction or disappearance of disease from involved area (in case where CT scan was used), and Deauville score (in case where PET-CT was used). Death during the study due to the disease effect was considered as part of treatment failure. Cases were followed at least yearly to estimate the rate of recurrence.

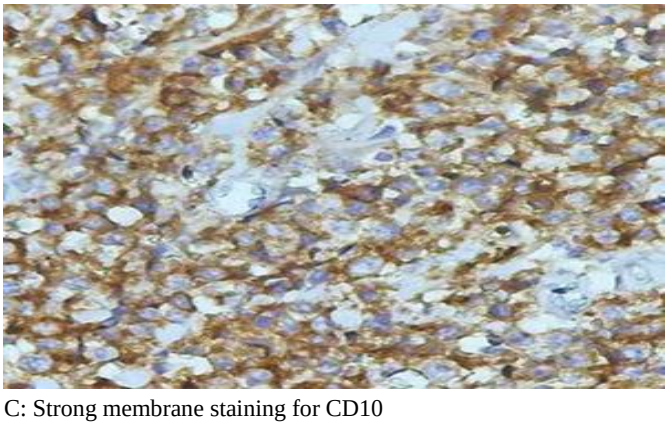
During immunohistochemistry study, five microns sections were obtained from formalin fixed-paraffin embedded tissue blocks and mounted on PathnSitu and Leica positively charged slides. For immunohistochemical staining evaluation, the slides were examined at 400x magnification for all patients. The lymphoma cases were classified into 2 groups based on COO, according to Hans et al into GCB or ABC. Cases were assigned to the GCB group in case that CD10 and/or BCL6 were positive with absence of MUM1/IRF4 expression. On the other hand, the lymphoma cases were classified as the ABC subgroup, when the nuclear staining for MUM1/IRF4 coincident with lack of CD10 &/or BCL6 expression by the same lymphoma cells. All slides were examined by expert histopathologist at Medical City Complex, Teaching Laboratories.



A: Large tumor cells



B: Strong membrane staining for CD20



C: Strong membrane staining for CD10

Figure 1: An example of DLBCL-GCB histology with immunohistochemistry, that showed positive staining for both CD10 and CD20.

Definitions:

The Eastern Cooperative Oncology Group (ECOG) performance status, Grading 0-5, as published in American Journal of. Clinical Oncology was used to assess the performance status of the patients (7).

B symptoms: They are characterized by the presence of each of the subsequent elements: rapid and significant reduction in body weight exceeding 10% within the 6 months leading up to the initial assessment, without a clear cause; unexplained, chronic, or recurring fever with temperatures over 38 ◦C in the past month; episodes of profuse nocturnal sweats that have occurred repeatedly during the past month (8).

International Prognostic Index Score (IPI) : It was used to stratify the risk groups of the patients and calculated according to the prognostic factors of aggressive lymphoma that include age, Ann Arbor, lactate dehydrogenase, ECOG Performance Score and number of extra-nodal areas involved and accordingly, patients were classified into low, low intermediate, high-intermediate, and high-risk group (8).

Complete response (CR): The PET-CT scan was evaluated using a 5-domains scale, each domain scores either 1, 2, or 3. The presence or absence of a residual mass was also considered. A score of 1 indicates no uptake above the background, a score of 2 indicates uptake equal to or less than the mediastinum, and a score of 3 indicates uptake higher than the mediastinum but equal to or less than the liver. A score of 4 indicates uptake greater than the liver, and a score of 5 indicates uptake significantly higher than the liver. Alternatively, on the CT scan, the target nodes or nodal masses should regress to a size of 1.5 cm or smaller in their longest diameter (9).

Partial response (PR): It was represented by PET-CT score 4 or 5 with reduced uptake compared with baseline and residual mass(es) of any size. OR On CT ≥50% decrease in size of the nodes and extra-nodal sites (9).

Progressive disease: The PET-CT score of 4 or 5 indicates an elevated level of uptake compared to the initial scan, together with the presence of additional areas of high FDG activity that are indicative of lymphoma. This assessment can be done either throughout the course of treatment or at the end of it. Alternatively, during a CT scan, a node or lesion was considered abnormal if its longest diameter was greater than 1.5 cm and if there was an increase in either the longest diameter or the short diameter by 0.5 cm for lesions that are 2 cm or smaller, or by 1.0 cm for lesions that are larger than 2 cm.

In cases of splenomegaly, the length of the spleen must expand by more than 50% compared to its previous increase from the baseline measurement. If there is no preexisting splenomegaly, the spleen must increase in size by at least 2 cm from its initial measurement. Enlargement of the spleen, whether it is a new occurrence or has happened before. An assessable disease, regardless of its size, that can be clearly attributed to lymphoma and/or the bone marrow showing fresh or recurring involvement. These parameters were used to determine the progression instances in the recruited patients in this study (9).

No response or stable disease: It is defined by having a score of 4 or 5 without any noticeable change in FDG uptake from the initial measurement during interim or end of treatment, as determined by PET scan. Additionally, there should be a decrease of less than 50% in measurable nodes and extra-nodal sites compared to the baseline. The criteria for progressive disease should not be met in target nodes/nodal masses or extr- nodal lesions. Furthermore, there should be no increase in organ enlargement that indicates disease progression, and no new lesions should appear (10).

The duration of follow-up for each patient was determined from the time of diagnosis until the interim evaluation, completion of treatment, and conclusion of the study. If a complete remission occurred, the follow-up period spanned from the time of diagnosis until the completion of the research, encompassing the duration of the remission. The follow-up period was determined from the time of diagnosis to the assessment at the midcourse evaluation and at the completion of therapy, considering progression, partial remission, and stable disease. The duration of follow-up in relapse cases ranged from the time of diagnosis to the date of confirmed relapse (10).

Prior to data collection, explicit agreement was sought from each patient in a formal manner, and the information gathered was kept anonymous. Names were substituted with identifying codes. All data was securely stored in a password-protected laptop and solely utilized for research purposes while maintaining strict confidentiality.

Study approval was obtained from the Council of Iraqi Board of Medical Specialization. Furthermore, the Scientific Committee at Baghdad National Centre of Haematology at Baghdad Teaching Hospital, Medical City granted approval.

Statistical analysis: All data were introduced into Microsoft Excel 16 and statistical analysis was conducted using IBM-SPSS (USA Chicago). Data were presented in the form of counts, percentage, mean, standard deviation (SD), minimum (Min) and maximum (Max) and presented in the form of tables, charts, or graphs. Testing of the level of significance of the categorical data was conducted using Chi square or Fisher exact test while continuous variables were tested using student t test or Mann Whitney u test whenever it was appropriate. Logistic regression analysis was used to examine the multivariate analysis for estimation of predictors of CR. Survival analysis was done using Kaplin-Mier analysis, while comparison of the groups of immunohistochemistry (IHC) regarding survival was done by using Log rank analysis. The predictors of survival were examined using Cox hazard regression analysis. Statistical significance was set at P value <0.05.

Results

The study included 134 cases, and of them 25 cases (18.7%) were shown by immunohistochemistry GCB, while 109 cases (81.3%) were shown by immunohistochemistry non- GCB.

Regarding the comparison of patient characteristics according to immunohistochemistry, there was no statistically significant difference in age group at presentation and gender of the participants. Cases of GCB had higher rates of early-stage disease than ABC which was presented in more advanced stages. This association was statistically significant.

Cases of GCB were found to be associated with lower IPI risk than ABC group. This association was statistically significant.

The presence of a mediastinal mass has no statistically significant association with either of the two groups. The B symptoms were not different according to the immunohistochemistry. The mean LDH level was also not different regarding immunohistochemistry. Further details are illustrated in Table 1.

The response to treatment was statistically different between the two groups and the rate of complete response was higher in cases of GCB than ABC while non-CR was associated with ABC immunohistochemistry. Mortality was not different between the two groups, as shown in Table 1.

To estimate the predictors of complete response, we applied binary logistic regression analysis which showed that the single independent predictor of complete response was the IPI score rather than COO or other factors, as shown in Table 2.

Table 1: Characteristics of the subtypes.

Variables		GCB		ABC		P value
		No.	%	No.	%	
Age group	<60 years	15	60.0	62	56.9	0.776
	≥60 years	10	40.0	47	43.1	
Gender	Male	17	68.0	65	59.6	0.439
	Female	8	32.0	44	40.4	
Stage	Early stage	7	28.0	8	7.3	0.003
	Advanced stage	18	72.0	101	92.7	
IPI	Low	11	44.0	19	17.4	0.039
	Low-intermediate	6	24.0	37	33.9	
	High-intermediate	5	20.0	36	33.0	
	High	3	12.0	17	15.6	
Mediastinal mass	Yes	1	4.0	11	10.1	0.336
	No	24	96.0	98	89.9	
B symptoms	Yes	24	96.0	101	92.7	0.547
	No	1	4.0	8	7.3	
LDH	Mean ±SD	409.9 ±200.4		476.9 ±369.4		0.215
Response	CR	19	76.0 %	52	47.7 %	0.011
	Non-CR	6	24.0 %	57	52.3 %	
Death	Yes	5	20.0 %	23	21.1 %	0.903
	No	20	80.0 %	86	78.9 %	

* ABC: Activated B-cell; CR: Complete response; GCB: Germinal center B-cell; IPI: International Prognostic Index Score; LDH: Lactate dehydrogenase.

Table 2: Multivariate analysis of factors that affect complete response.

Variables		CR (n=71)		Non-CR (n=63)		P value
		No.	%	No.	%	
Age group	<60 years	42	59.2	35	55.6	0.091
	≥60 years	29	40.8	28	44.4	
COO	GCB	19	26.8	6	9.5	0.140
	ABC	52	73.2	57	90.5	
Stage	Early stage	15	21.1	0	0.00	0.999
	Advanced stage	56	78.9	63	100	
IPI	Low	28	39.4	2	3.2	0.007
	Low-intermediate	23	32.4	20	31.7	
	High-intermediate	12	16.9	29	46	
	High	8	11.3	12	19	
B symptoms	Yes	62	87.3	63	100	N/A
	No	9	12.7	0	0	
LDH	Mean ±SD	377.66	176.57	562.14	448.57	0.252

* ABC: Activated B-cell; COO: Cell of origin; CR: Complete response; GCB: Germinal center B-cell; IPI: International Prognostic Index Score; LDH: Lactate dehydrogenase; N/A: Not applicable.

Survival analysis showed that the COO had no effect on either progression-free survival (PFS) or overall survival (OS). The mean PFS in months in cases of GCB was 11.6±1.5 months while the mean PFS was 9 ±0.7 months in ABC cases. The mean overall survival rate of cases of GCB was 15.9±1.5 months, while it was 17±0.7 months in ABC cases, as shown in Table 3, Figure 2, and Figure 3.

Table 3: Survival analysis in the cases studied.

Progression free survival in months					
COO	Mean ±SD	95% CI	Min	Max	P value
GCB	11.6 ±1.5	8.7-14.6	4	20	0.108
ABC	9.0 ±0.7	7.7-10.3	2	21	
Overall survival in months					
GCB	15.9 ±1.5	12.9-18.8	4	20	0.885
ABC	17.0 ±0.7	15.5-18.4	2	21	

* ABC: Activated B-cell; CI: Confidence interval; COO: Cell of origin; GCB: Germinal center B-cell.

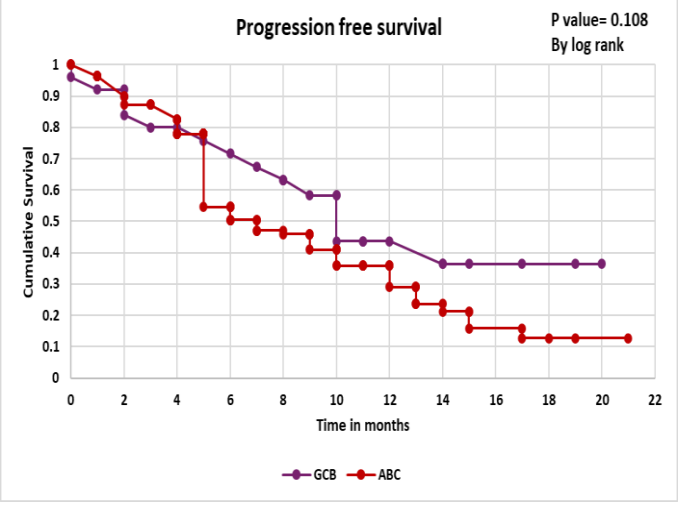


Figure 1: Progression free survival using Kaplan-Meier analysis.
* ABC: Activated B-cell; GCB: Germinal center B-cell**.**

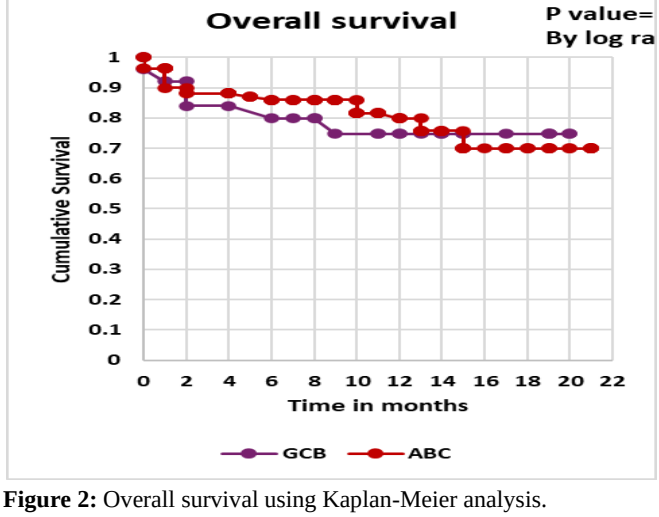


Figure 2: Overall survival using Kaplan-Meier analysis.
* ABC: Activated B-cell; GCB: Germinal center B-cell.

For estimation of predictors of the survival, we applied univariate and multivariate (cox regression analysis) analysis and found that the single independent predictor of progression-free survival was IPI and

the single independent predictor of overall survival was LDH level, as shown in Table 4 and Table 5, respectively.

Table 4: Predictors of progression-free survival by univariate and multivariate analysis.

Predictors		Survived No. (%)	Non-survival* No. (%)	P value	
				Univariate	Multivariate
Age	Mean ±SD	52.65 ±16.59	52.98 ±15.53	0.913	0.077
COO	GCB	11 (23.9)	14 (15.9)	0.259	0.825
	ABC	35 (76.1)	74 (84.1)		
Stage	Early stage	11 (23.9)	4 (4.5)	0.001	0.930
	Advanced stage	35 (76.1)	84 (95.5)		
IPI	Low	22 (47.8)	8 (9.1)	<0.0001	0.007
	Low-intermediate	13 (28.3)	31 (35.2)		
	High-intermediate	7 (15.2)	33 (37.5)		
	High	4 (8.7)	16 (18.2)		
LDH	Mean ±SD	330.72 ±140.75	534.27 ±396.11	<0.0001	0.235
B symptoms	Yes	44 (95.7)	81 (92)	0.428	0.884
	No	2 (4.3)	7 (8)		

* Progressive disease or death.
** ABC: Activated B-cell; CR: Complete response; COO: Cell of origin; GCB: Germinal center B-cell; IPI: International Prognostic Index Score; IHC: Immune histochemistry; LDH: Lactate dehydrogenase.

Discussion

Diffuse large B-cell lymphoma (DLBCL) is a neoplasm of medium-large B lymphoid cells with diffused growth patterns. Although it is a potentially curable disease, around 40% of the cases are either refractory to primary treatment or relapse. Based on gene expression profiling (GEP), DLBCL can be classified as germinal center B-cell subtype (GCB) and activated B-cell subtype (ABC). About 10%–15% of cases do not convincingly fall into either of the two subtypes and hence remain unclassified. Most widely used and suggested by WHO is Hans's algorithm comprising immunohistochemical markers CD10, B-cell lymphoma6 (BCL6), and IRF4/MUM1, which classifies CD10+ and CD10-/BCL6+/MUM1-DLBCL as GCB, while CD10-/BCL6+/MUM1 + and BCL6-DLBCL as non-GCB (11). There are conflicting results regarding the significance of COO in the response to frontline treatment, and effect on survival. In this study, we investigated the role of COO (that is diagnosed by immunohistochemistry) on patient survival and outcome and compared the presentations of these subtypes.

Table 5: Predictors of overall survival by univariate and multivariate analysis.

Predictors		Survived No. (%)	Death No. (%)	P value	
				Univariate	Multivariate
Age	Mean ±SD	52.22 ±15.98	55.21 ±15.36	0.363	0.603
COO	GCB	19 (18.1)	6 (20.7)	0.751	0.516
	ABC	86 (81.9)	23 (79.3)		
Stage	Early stage	13 (12.4)	2 (6.9)	0.407	0.581
	Advanced stage	92 (87.6)	27 (93.1)		
IPI	Low	25 (23.8)	5 (17.2)	0.412	0.998
	Low-intermediate	36 (34.3)	8 (27.6)		
	High-intermediate	31 (29.5)	9 (31)		
	High	13 (12.4)	7 (24.1)		
LDH	Mean ±SD	411.67 ±232.45	655.31 ±561.42	0.029	0.008
B symptom	Yes	96 (91.4)	29 (100)	N/A	N/A
	No	9(8.6)	0 (0)		

* ABC: Activated B-cell; CR: Complete response; COO: Cell of origin; GCB: Germinal center B-cell; IPI: International Prognostic Index Score; IHC: Immune histochemistry; LDH: Lactate dehydrogenase.

The study included 134 participants, 18.7% of participants were diagnosed as being GCB, and the remaining 81.3% were ABC. The age of presentation was 57.5% among those over the age of 60 years. Nair et al (12) found that rate of cases presented with age older than 65 years was 28.45%. Johnson et al (13) found that the number of cases of DLBCL among those older than 70 years was increasing, and this would put the patients at increased risk according to age as older patients had inferior survival and increased risk of drug toxicity with decreased performance status and multiple comorbidities.

In the present study, the gender of the patients was 61.2% males and 38.2% females. Keloth Kavya et al (14) found the male involvement to be 60% and females 40%. The stage at presentation in our study was mainly stage IV (54.5%), Rodrigues-Fernandes et al (15) found in their systematic review on DLBCL-NOS that the presentation was mainly late with aggressive nature of disease.

The intermediate risk (based on IPI score) was the most frequent finding at time of presentation in the current study. Most cases

(93.3%) had B symptoms at presentation. The mean LDH at time of presentation was 464.4 ±344.6 U/L.

The COO showed no difference in regard to age of presentation in our study. A similar result was found by Desai et al (16) and Wawire et al (17). There was no difference in regard to gender according to COO. A similar finding was reported by Desai et al (16) and Wawire et al (17).

The stage of presentation was different according to COO, as 92.7% of cases of ABC presented with advance stage. Kerian et al (18) found a similar result. While Desai et al (16) found that 74.9% of the cases of DLBCL had advanced stage, while no difference in regard to COO. This contradiction to the current study probably happened as Desai et al[(16)] they included cases of unknown COO (IHC not done) in their analysis.

The IPI score was different between the two studied groups. Cases of ABC had higher IPI score than cases of GCB. Bettelli et al (19) reported similar results. Desai et al (16) found that IPI had no significant association with COO. This difference probably happened due to the inclusion of cases of unknown COO (IHC not done) in the analysis.

The presence of mediastinal mass was not different according to COO. This correlation was poorly investigated in the literature.

The presence of B symptoms was not different according to COO. Similar results were found by Abdulla et al (20) while Bettelli et al (19) found that ABC cases had higher rate of B symptoms. This probably happened due to the high number of cases of B symptoms in the current study, with only nine cases without B symptoms which increases the probability of type II error.

The mean LDH level was not different according to COO. Similar results found by Abdulla et al 920) and Desai et al (19).

Regarding achieving CR, GCB cases showed a higher rate of CR when compared with ABC cases. But after applying multivariate analysis, we found that complete response was not dependent on the COO. In fact, IPI was the single independent predictor of complete response. Similarly, Gogia et al (21), Chowdhury et al (22), and Kerian et al (18) found that COO had no effect on CR rate. However, Tyagi et al (23) found a significant association of GCB with increased CR rate. This result was noticed on univariate analysis found in the current study but the application of multivariate analysis (regression analysis) had lessen the effect of COO on CR rate. Such analysis was not done by Tyagi et al (23) who found a significant association of IPI with CR rate. This observation supports our findings on multivariate analysis. Warnnissorn et al (24) found that IPI score is a reliable predictor of CR in DLBCL cases.

Regarding survival analysis, COO showed no difference in either disease free survival or overall survival. Lee et al (25) found in their study that including cases of DLBCL and dividing according to both Hans algorithm and Lymph2Cx into cases of GCB and cases of ABC and after five years follow-up showed no difference in the survival.

Further analysis of factors that affect survival using multivariate analysis (cox regression analysis) showed that the single independent predictor of PFS was IPI score with no effect from the COO. The overall survival on the other hand was dependent on LDH level only, with no effect from the COO. Nair et al (12) found no effect of COO on the three years event free survival; however, they found that IPI is a good predictor of survival at three years of follow-up. Desai et al (16) and Gogia et al (21) also found no significant difference in two years and three years overall survival, respectively depending on COO. Bettelli et al (19) found that IPI is an independent predictor of survival, and not COO. Abdulla et al (20) found that ABC cases by Hans algorithm were not different from cases of GCB in regard overall survival. However, on doing Lymph2Cx, they found that ABC cases had significantly lower survival than GCB. The progression free survival was significantly lower in ABC cases by both Hans algorithm and Lymph2Cx, than GCB cases. This difference may be attributed to multiple factors. First, the use of Lymph2Cx which had a superior detection rate of ABC cases than Hans's algorithm. This was supported by Cho et al (26) who found no difference in survival according to Has algorithm, but inferior survival of ABC according to Lymph2Cx. Second, the multivariate analysis in their study included neither LDH level nor IPI score which was found to be cofounders in our study and their elimination resulted in a non-significant association of COO with survival. Furthermore, their study had a larger sample size (n=351) and longer follow-up period (five years).

Conclusion

COO exhibited no effect on response to treatment and had no survival benefits. The IPI score was found to be a good predicter of complete response and survival.

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Conflict of Interest

Authors declare no conflict of interest.

Data availability

Data are available upon reasonable request.

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References

[1] HG Watson, DJ Culligan, Manson L. Haematology and transfusion medicine. In: Stuart H Ralston, Ian D Penman, Mark WJ Strachan, Hobson RP, editors. Davidson's Principles and Practice of Medicine. 24th ed. Amsterdam, Netherlands: Elsevier; 2022, pp. 964-6.

[2] Sehn LH, Salles G. Diffuse Large B-Cell Lymphoma. N Engl J Med. 2021Mar;384(9):842-58. http://doi.org/10.1056/nejmra2027612.

[3] Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, et al. Global Cancer Observatory: Cancer Today Lyon, France: : International Agency for Research on Cancer; 2020. Available from: https://gco.iarc.fr/today.

[4] Ott G, Ziepert M, Klapper W, Horn H, Szczepanowski M, Bernd H-W, et al. Immunoblastic morphology but not the immunohistochemical GCB/nonGCB classifier predicts

outcome in diffuse large B-cell lymphoma in the RICOVER-60 trial of the DSHNHL. Blood. 2010 Dec;116(23):4916-25. http://doi.org/https://doi.org/10.1182/blood-2010-03-276766.

[5] Susanibar-Adaniya S, Barta SK. 2021 Update on Diffuse large B cell lymphoma: A review of current data and potential applications on risk stratification and management. Am J Hematol. 2021May;96(5):617-29 http://doi.org/10.1002/ajh.26151.

[6] Lavacchi D, Landini I, Perrone G, Roviello G, Mini E, Nobili S. Pharmacogenetics in diffuse large B-cell lymphoma treated with R-CHOP: Still an unmet challenge. Pharmacol Ther. 2022 Jan;229:107924. http://doi.org/https://doi.org/10.1016/j.pharmthera.2021.107924.

[7] Oken MM, Creech RH, Tormey DC, Horton J, Davis TE, McFadden ET, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol. 1982 Dec;5(6):649-55.

[8] Okosun J, Cwynarski K. Non-Hodgkin Lymphoma: High Grade. Postgraduate Haematology. 2015 Nov, Seventh Edition, pp:631-50. http://doi.org/https://doi.org/10.1002/9781118853771.ch34.

[9] Cheson BD, Ansell S, Schwartz L, Gordon LI, Advani R, Jacene HA, et al. Refinement of the Lugano Classification lymphoma response criteria in the era of immunomodulatory therapy. Blood. 2016 Nov;128(21):2489-96. http://doi.org/https://doi.org/10.1182/blood-2016-05-718528.

[10] Cheson BD, Fisher RI, Barrington SF, Cavalli F, Schwartz LH, Zucca E, et al. Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: the Lugano classification. J clin oncol. 2014 Sep;32(27):3059-68. http://doi.org/https://doi.org/10.1200/JCO.2013.54.8800.

[11] Dhar L, Singh S, Jain SL, Vindal A, Sinha P, Gautam R. Cell of origin classification of diffuse large B-Cell lymphoma. J Microsc Ultrastruct. 2023 Jan;12(4):193-8. http://doi.org/10.4103/jmau.jmau_66_22.

[12] Nair R, Bhurani D, Rajappa S, Kapadia A, Reddy Boya R, Sundaram S, et al. Diffuse Large B-Cell Lymphoma: Clinical Presentation and Treatment Outcomes From the OncoCollect Lymphoma Registry. Front Oncol. 2022 Feb;11: 796962. http://doi.org/10.3389/fonc.2021.796962.

[13] Johnson PC. Frailty and Diffuse Large B-Cell Lymphoma: Where Do We Go From Here? J Natl Compr Canc Netw. 2022 Jun;20(6):735-6. http://doi.org/10.6004/jnccn.2022.7031.

[14] Keloth Kavya A, K Nair C, Padmanabhan M, Raghavan Sindhu E. Evaluation of Haematological Parameters and Lymphocyte Monocyte Ratio as a Prognostic Marker in Diffuse Large B-cell Lymphoma and T Cell Lymphoma Patients- An Observational Study. Asian Pacific J Cancer Care. 2022 Oct;7(4):607-13. http://doi.org/10.31557/apjcc.2022.7.4.607-613.

[15] Rodrigues-Fernandes CI, de Souza LL, Santos-Costa SFd, Pontes HAR, de Almeida OP, Vargas PA, et al. Clinicopathological analysis of oral diffuse large B-cell lymphoma, NOS: A systematic review. J Oral Pathol Med. 2019 Mar;48(3):185-91. http://doi.org/https://doi.org/10.1111/jop.12802.

[16] Desai SH, Mwangi R, Smith AN, Maurer MJ, Farooq U, King RL, et al. Cell of origin is not associated with outcomes of relapsed or refractory diffuse large B cell lymphoma. Hematol Oncol. 2023 Feb; 41(1):39-49. http://doi.org/10.1002/hon.3098.

[17] Wawire J, Sayed S, Moloo Z, Sohani AR. Diffuse Large B-Cell Lymphoma in Kenya: MYC, BCL2, and the Cell of Origin. J Glob Oncol. 2019 Mar;5:1-8. http://doi.org/10.1200/jgo.18.00203.

[18] WAW WN, Azlan H, Faezahtul AH. Classifying DLBCL according cell of origin using Hans algorithm and its association with clinicopathological parameters: A single centre experience. Med J Malaysia. 2020 Mar 1;75(2):98-102.

[19] Bettelli S, Marcheselli R, Pozzi S, Marcheselli L, Papotti R, Forti E, et al. Cell of origin (COO), BCL2/MYC status and IPI define a group of patients with Diffuse Large B-cell Lymphoma (DLBCL) with poor prognosis in a real-world clinical setting. Leuk Res. 2021May;104:106552. http://doi.org/https://doi.org/10.1016/j.leukres.2021.106552

[20] Abdulla M, Hollander P, Pandzic T, Mansouri L, Ednersson SB, Andersson PO, et al. Cell-of-origin determined by both gene expression profiling and immunohistochemistry is the strongest predictor of survival in patients with diffuse large B-cell lymphoma. Am J Hematol. 2020 Jan;95(1):57-67. http://doi.org/10.1002/ajh.25666.

[21] Gogia A, Nair S, Arora S, Kumar L, Sharma A, Gupta R, et al. Impact of Cell-of-Origin on Outcome of Patients With Diffuse Large B-Cell Lymphoma Treated With Uniform R-CHOP Protocol: A Single-Center Retrospective Analysis From North India. Front Oncol. 2021 Dec;11: 770747. http://doi.org/10.3389/fonc.2021.770747.

[22] Chowdhury ZZ, Bahar T, Rahman S, Haque S, Islam AM, Ali M, et al. Outcome of Diffuse Large B-Cell Lymphoma with First-line Chemotherapy. Haematol J Bangladesh. 2021;5(1):3-9. http://doi.org/10.37545/haematoljbd202156.

[23] Tyagi A, Abrari A, Khurana A, Tyagi S. Immunohistochemical subtyping of diffuse large B-cell lymphoma into germinal center B-cell and activated B-cell subtype, along with correlation of the subtypes with extranodal involvement, serum lactate dehydrogenase, and positron emission tomography scan-based response assessment to chemotherapy. J Cancer Res Ther. 2022 Jul;18(4):1129-36. http://doi.org/10.4103/jcrt.JCRT_842_20.

[24] Warnnissorn N, Kanitsap N, Niparuck P, Boonsakan P, Kulalert P, Limvorapitak W, et al. External validation and

comparison of IPI, R-IPI, and NCCN-IPI in diffuse large B-cell lymphoma patients treated with R-CHOP to predict 2-year progression-free survival. Hematology. 2022 Dec;27(1):1237-45. http://doi.org/10.1080/16078454.2022.2147916.

[25] Lee J, Hue SS-S, Ko SQ, Tan SY, Liu X, Girard L-P, et al. Clinical impact of the cell-of-origin classification based on immunohistochemistry criteria and Lymph2Cx of diffuse large B-Cell lymphoma patients in a South-east Asian population: a single center experience and review of the literature. Expert Rev Hematol. 2019 Dec;12(12):1095-105. http://doi.org/10.1080/17474086.2019.1677152.

[26] Cho I, Yoon N, Hyeon J, Sim J, Yoo HY, Kim SJ, Kim WS, Ko YH. Comparison of the lymph2Cx assay and Hans algorithm in determining the cell-of-origin of diffuse large B-cell lymphomas, not otherwise specified. Appl Immunohistochem Mol Morphol. 2020 Nov;28(10):731-40. http://doi.org/10.1097/pai.0000000000000843.

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