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Original Articles

Clinicopathological Correlation with Outcome of Diffuse Large B Cell Lymphoma: Experience in a Specialized Cancer Care Centre in Bangladesh

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Abstract

***Background**: Diffuse large B-cell lymphoma (DLBCL) is the most common type of non-Hodgkin lymphoma (NHL) in the world, and accounts for 30%–40% of all adult NHLs. It is clinically, morphologically and genetically a heterogeneous group of tumors composed of large B cells. This study aimed to determine the clinical features, treatment options, the response rate in a specialized cancer care centre.*

***Methods**: This retrospective study included all DLBCL patients registered in the department of Haematology of National Institute of Cancer Research and Hospital (NICR&H), Bangladesh between July 2016 to June 2019.*

rate (ORR) was 76.6% and 9.2% of death. The response was found to be significant with B symptoms, stage, and international prognostic index (IPI) score. But no significant difference was observed in outcome among different types of DLBCL after treatment.

***Conclusion:** This retrospective study will help to ascertain the co relation of DLBCL outcome with clinicopathological profile. (edited)*

***Keywords**: Diffuse large B-cell lymphoma, non-Hodgkin lymphoma, outcome, Bangladesh.*

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Introduction:

Diffuse large B-cell lymphoma (DLBCL) is a heterogeneous, aggressive group of non-Hodgkin's lymphoma (NHL), characterized by proliferation of large neoplastic B cells.[1] The biological and clinical heterogeneity of DLBCL has already been recognized in the Revised European-American Lymphoma (REAL) and World Health Organization (WHO) classifications.[2,3] Patients most often present with a rapidly growing tumor mass in single or multiple, nodal or extra-nodal sites. Since the 1970 Cyclophosphamide, Doxorubicin, Vincristine, and Prednisolone (CHOP) regimen are used as a standard treatment for NHL.[2,4] With this conventional chemotherapy more than half of the cases of DLBCL can be cured. Recently integration of Rituximab has become a standard of care for patients with DLBCL.[1,5,6] But its widespread use in developing countries is still limited by the lack of financial coverage.[7,8]. However, most of the patients die because of having tumors that are either refractory to the currently available treatment or due to relapse after a period of remission.[9,10] Various factors like patient's age, performance status, disease extension and growth, biochemical markers, clinical-stage can predict the

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patient's prognosis and outcome after chemotherapy. Four discrete outcome groups were identified depending on these factors in the international prognostic index (IPI) of DLBCL with five years overall survival ranging from 32% to 83%.[1,6]

In Bangladesh, unfortunately, no specific data is found to see the incidence and outcome of DLBCL. Therefore, this study aimed to determine the clinical course, treatment options, response rate with first-line chemotherapy.

Methods:

This retrospective study was carried out in the Haematology Department of National Institute of Cancer Research and Hospital (NICRH). We enrolled diagnosed and registered cases of DLBCL aged >16 years from July 2016 to June 2019.We excluded secondary lymphomas, HIV associated lymphoma, patients with incomplete records. The patients were classified as germinal centre B like (GCB) or activated B cell type using the Hans classification.[2,3] Analysis was carried out using statistical package for the social sciences (SPSS) version 24. Chi-square test was used to extract *p*-value.

Results:

The clinical profile of the patients indicated a male to female ratio of 1.96, while the mean age was 47(±15) years.

Extranodal involvement was seen in 16.56% patients. The most frequently affected sites were the stomach and intestine followed by the central nervous system (CNS). The other sites were testis, bone, thyroid, renal, skin and soft tissue. Most of the patients were managed with CHOP (94.7%)± Rituximab and rarely with Cyclophosphamide, Vincristine, Prednisolone (CVP) (0.7%), Cyclophosphamide, Etoposide, Procarbazine, Prednisolone (CEPP) (1.3%), Etoposide, Prednisolone, Vincristine, Cyclophosphamide, Doxorubicin (EPOCH) (2.6%). Rituximab was used in 21.9% and triple intrathecal therapy (TIT) was used in 15.9%. The median chemotherapy cycle used was six. A positron emission tomography (PET) scan was used for the evaluation of response. The overall response rate (ORR) was 76.16% and complete remission (CR) was 42.38%. CR rate was better with low and intermediate IPI. With a median follow up of 24 months (6-48month), a total of 36 events occurred, including relapse, refractory, and death.

Table 1: *Demographic and clinical features of 151 patients diagnosed with diffuse large B cell lymphoma*

Features	N (%)
Age	
<60	115 (76.16)
>60	36 (23.84)
Gender	
Male	100 (66.2)
Female	51 (33.8)
Primary site	
Nodal	126 (83.44)
Extra nodal	25 (16.56)
Subtype	
GCB	48 (31.8)
Non-GCB	70 (46.4)
NOS*	33 (21.9)
B symptoms	
Present	77 (50.99)
Absent	74 (49.01)
Bone marrow involvement	
Present	4 (2.6)
Absent	147 (97.4)
Stage	
1	28 (18.54)
2	57 (37.75)
3	60 (39.73)
4	6 (3.97)
IPI	
Low risk	50 (33.11)
Intermediate risk	95 (62.91)
High risk	6 (3.97)

*NOS= Not otherwise specified

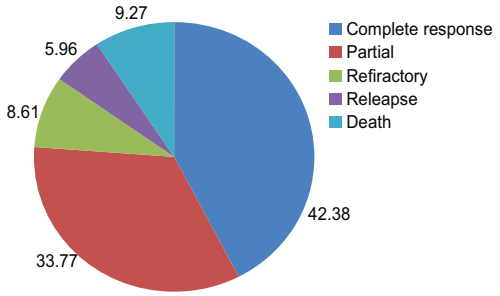

Figure 1: Outcome of initial treatment (n=151)

The response was compared with clinicopathological parameters and the p-value was found significant with B symptoms, stage, and IPI score.

Table 2: *B symptoms with outcome (n=151)*

	CR (N%)	PR(N%)	Refractory(N%)	Relapse(N%)	Death(N%)	p-value
Present	25(16%)	26(17.21%)	9(5.96%)	5(3.31%)	12(7.94%)	
Absent	39(25.82%)	25(16%)	4(2.64%)	4(2.64%)	2(1.32%)	.016
Total	64(42.38%)	51(33.77%)	13(8.61%)	9(5.96%)	14(9.27%)	

*PR=partial response

Table 3. *Stage with outcome (n=151)*

Stage	CR (N%)	PR (N%)	Refractory (N%)	Relapse (N%)	Death (N%)	p-value
I	25(16%)	2(1.32%)	1(.66%)	0(0%)	0(0%)	
II	24(15.89%)	22(14.56%)	4(2.64%)	3(1.986%)	4(2.64%)	
II	14(9.27%)	23(15.23%)	8(5.29%)	6(3.97%)	9(5.96%)	.009
IV	1(.66%)	4(2.64%)	0(0%)	0(0%)	1(.66%)	
Total	64(42.38%)	51(33.77%)	13(8.61%)	9(5.96%)	14(9.27%)	

Table 4. *IPI with outcome (n=151)*

IPI	CR (N%)	PR (N%)	Refractory (N%)	Relapse (N%)	Death (N%)	p-value
0	44(2.64%)	44(2.64%)	0(0%)	0(0%)	0(0%)	
1	26(17.21%)	9(5.96%)	44(2.64%)	1(.66%)	2(1.32%)	
2	24(15.89%)	2424(15.89%)	7(4.63%)	6(3.97%)	3(1.98%)	
3	7(4.63%)	12(7.94%)	2(1.32%)	1(.66%)	9(5.96%)	<0.001
4	3(1.986%)	2(1.32%)	0(0%)	0(0%)	0(0%)	
5	0(0%)	0(0%)	0(0%)	1(.66%)	0(0%)	
Total	64(42.38%)	51(33.71%)	13(8.61%)	9(5.96%)	14(9.27%)	

Discussion:

DLBCL is the most common subtype of NHL worldwide.[2,7,8] In our study we analyzed 151 cases of DLBCL. Age distribution was almost a decade and a half-year younger to those reported in developed world[1,3] and similar to developing countries.[6,7,11] [Table 1] The younger average age of Bangladeshi patients correlates with the pattern seen in most other malignancies due to the effect of a younger population or due to referral bias toward younger patients for treatment at the higher centre.[6,8] Non-GCB was the most common subtype found in our patient followed by GCB which is similar to that of western countries[1,5,12] and slightly differs from that of India[6,8,9]. Age of the patients is an indicator prognostic factor as patients younger than 60 years have a better prognosis.[11,13]

Another method for prognostic assessment is the IPI score, which includes some of the factors listed above, a scoring system that was used long before the introduction of rituximab as therapy for the NHL. In the current practice, it still remains the easiest prognostic score due to the information that can be rapidly obtained but also due to its relative ability to predict the outcome, which has been demonstrated in various studies.[11-15] Even if the risk stratification by IPI is more accurate than Ann Arbor staging, this scoring system alone is not fully consistent with the disease outcome.

One of the potential limitations of our study resides in the heterogeneity of DLBCL patients in terms of treatment regimen. 94.7% got CHOP but only 21.9% had rituximab.

In this study, we have tried to verify the degree of concordance of IPI score with other potential risk factors for disease outcomes. The results point out to a significant correlation between IPI high risk (3-5) subgroup and unfavorable clinical and therapeutic outcomes (presence of B-symptoms, refractory disease). [Table 4] Patients with high and intermediate IPI had low CR as compared to patients with low IPI.[1,8,10] Presence of B symptoms had less CR similar to other counties.[8,9,12-14] [Table 2] Among the subtypes non-GCB had an unfavorable prognosis, so the choice of treatment for this subtype should be carefully considered. Some studies have shown that some treatments have greater efficacy in recurrent or refractory patients with non-GCB subtype than those with GCB subtype.[1,10,13]

Overall response rate and CR were inferior to other countries which may be due to economic constraint, lack of specialized cancer care center, lack of trained doctor, heterogeneity of treatment, and lack of awareness.[1,6,8,11]

The study is limited due to its retrospective nature, a limited number of data and the short follow up period. Even though a single centre study, it provides information about clinical features and treatment outcome of DLBCL in Bangladesh.

Conclusion:

The implementation of DLBCL cell-of-origin classification according to Hans algorithm and IPI score is essential, as both predictors positively correlate with several clinico-pathological parameters and outcomes.

Area of conflict:

The authors declare no financial or nonfinancial conflict of interest.

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