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Clinical Spectrum and Subtype Distribution Lymphoma : A Single Center, Hospital Based Analysis

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Summary:

Introduction: Lymphoma is a heterogeneous group of hematological malignancy that varies in different subtypes according to geography, age, race and ethnicity. In this study, the different subtype of lymphoma according to WHO lymphoid tumor classification and clinical features of Non Hodgkins lymphoma will be analyzed and discussed at a tertiary care Hematology center.

Objectives: Our aims and objective is to observe and share the single center experience of specifically Non-Hodgkin lymphoma and to contribute in formation of national lymphoma registry in future to enhance the care of potentially curable lymphomas.

Materials and Method: A retrospective analysis of 226 diagnosed lymphoma cases were conducted at DMCH Hematology center from January 2016 to September 2017(total 21 months period). Data were reviewed and analyzed using simple frequency and percentage. Protocol was approved by institutional ethical review board (IRB) of DMCH.

Result: The mean age of NHL is 43 (12-90) years with majority of patients were in 31-55 years age group and M:F is 3:1. The mean age of HL is 30 (range 4-60) years without bimodal peak observed. Mixed cellularity classical HL were found higher than nodular sclerosis HL.

Majority of NHL were B cell NHL (86.25%) and remaining were T cell NHL (13.75%).

The most common variant found was aggressive diffuse large B cell lymphoma(DLBCL) (48%), followed by peripheral T cell lymphoma PTCL (~13%) and very aggressive lymphoblastic lymphoma (LBL) (11%), low grade follicular Lymphoma (11%) and others (~17%).

70% NHL had nodal presentation and 30% had extra nodal involvement with GIT and CNS most commonly involved. Extra nodal presentations were more observed in DLBCL and LBL. Majority (75%) of NHL presented at advanced stage with B symptoms observed in 86% and variable IPI score. In DLBCL cell of origin was detected as non-GCB in 25(41%), GCB in 04(6%) and unclassifiable in 03(5%) cases according to Han's algorithm, and cell of origin was not detected in remaining cases.

Conclusion: This is a small scale retrospective study, this can lead raising awareness of doing large scale national data registry for various lymphoma patients. The thorough clinical and diagnostic information about lymphoma is necessary for better management and outcome.

Key words: HL, NHL, PTCL, DLBCL, GCB, non GCB, LBL.

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Introduction:

Lymphoid neoplasm originating from either B or T lymphocytes is heterogeneous both biologically and clinically. The incidence of lymphoma is increasing all over the world specially in western countries. A multicenter retrospective study reported that NHL and HL comprises 16.9% and 3.9 % among the hematological malignancies over a 5 years study period in Bangladesh.[1] Moreover different epidemiologic studies have shown considerable differences in the distribution of lymphoma subtypes between Asian and western populations.[2,3,4] Over the past few decades the classification of NHL has emergently being changed. World Health Organization (WHO) revised the consensus classification of lymphoma in 2001 and 2008. Finally WHO most recently updated the 2016 version that encompassed morphology, immunophenotype, biology of tumor and gene expression of lymphoma.[5] The therapy and prognosis of HL and NHL depend on the subtype, stage and associated co-morbid conditions. However there is lack of potential data of subtype distribution and clinical presentation pattern of both Hodgkins and non Hodgkin lymphoma in Bangladesh. The purpose of

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this paper is to observe and share the single centre experience of subtype distribution of all lymphoma and clinical features of only NHL .

Materials and Method:

A retrospective analysis of histopathologic and immunohistochemistry profiles and clinical features of different pattern of diagnosed 226 lymphoma cases were conducted who attended at DMCH Hematology center from January 2016 to September 2017(total 21 months period). Data were analyzed and reviewed and expressed as frequency and simple percentage. The protocol of this study was approved by the institutional ethical review board (IRB) of Dhaka Medical College Hospital.

Result:

A total 226 Lymphoma patients were included in this study who attended at Hematology department of DMCH from different parts of the country. Out of total 226 lymphoma cases 160 patients were NHL and 66 were HL. The mean age of HL is 30 (range 4-60) years without bimodal peak observed. Among the HL, 24 (36.6%) were mixed cellularity, 5 (7%) were nodular sclerosis and in 32(48%) cases histopathologic subtype were not mentioned, rather reported as classical HL. Nodular lymphocyte predominant HL(NLPHL) and lymphocyte depleted variety were observed in 5 cases (3 & 2 respectively). All these HL cases were being confirmed by immunohistochemistry (IHC).

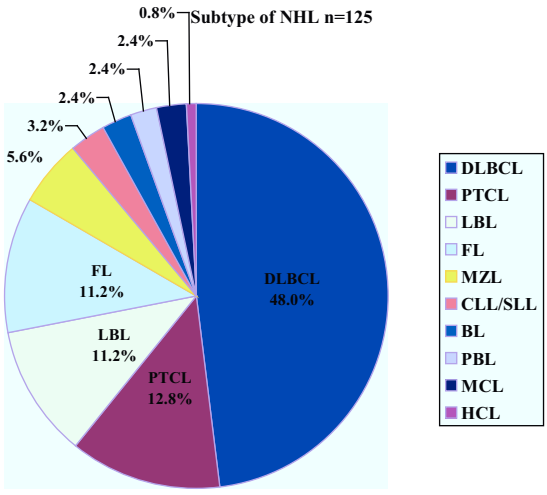
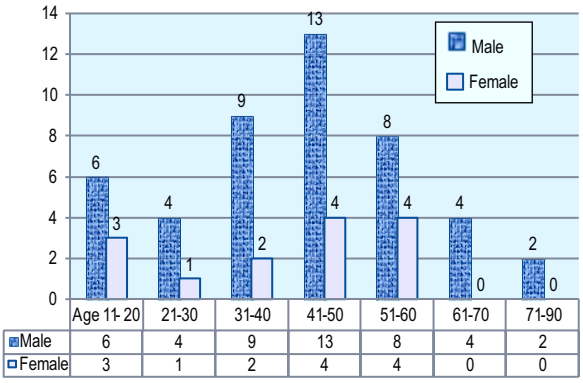


Fig.-1: *Different subtype distribution of NHL according to WHO classification.*

Among the 160 NHL patients, 138 (86.25%) cases were B cell type and remaining 22(13.75%) cases were T cell type.

Median age at diagnosis was 43(12-90) years and M:F ratio was 3: 1 for all NHL patients. Among the 160 NHL patients, 35 patients were not been able to be evaluated due to lack of proper data and lack of enough immuno-histochemitry profile . Finally 125 NHL patient's clinical parameters, histopathology, IHC and other investigations were evaluated. The most common variant was found is aggressive DLBCL (60/48.38%), followed by PTCL 16(12.8%), very aggressive lymphoblastic lymphoma (LBL) 14(11.2%), low grade follicular lymphoma 14(11.2%) and others 21 (16.42%) comprising marginal zone lymphoma, Mantle cell lymphoma, chronic lymphocytic leukemia/small lymphocytic lymphoma,



	Age 11-20	21-30	31-40	41-50	51-60	61-70	71-90
Male	6	4	9	13	8	4	2
Female	3	1	2	4	4	0	0

Fig 2: *Age and sex distribution of DLBCL(n=60)*

Hairy cell leukemia, plasmablastic lymphoma and Burkitts Lymphoma.

Most of the DLBCL (45/75%) patients presented with advanced stage III/IV disease, remaining 25% were detected at early I/II stage disease. Majority of these DLBCL patients (86%) had B symptoms at diagnosis. While almost all patients of lymphoblastic lymphoma (LBL) and PTCL had III/IV disease. Forty two (70 %) patients of DLBCL had nodal presentation and remaining 18 (30%) had extranodal presentation with or without nodal involvement, comprising most common extranodal site is GIT and CNS. Other rare extranodal sites were breast, paranasal sinus, soft palate, urinary bladder, tonsil, shoulder and testes. Very few of DLBCL(06/10%) had bone marrow involvement at

Table -I

Clinical presentation of major subtype of NHL

Patient profile	Number / percentage			
	DLBCL n=60	PTCL n =16	LBL n=14 n=14	FL
Age in Years:				
<60	50	13	14 07	
>60	10	03	00 07	
Range	(12-90)	(18-70)	(14-28)	(30-69)
Sex				
Male	45	14	10 10	
Female	15	02	04 04	
M:F ratio	3:1	7:1	2.5:12.5:1	
B symptoms:	52(86%)	15(93%)	14(100%)	07(50%)
Fever /Night sweats /weight loss				
Lymph node enlargement				
• Cervical± Supraclavicular	50	13	09 11	
• Axillary	20	08	06	
• Mediastinal	12	05	08	
• Abdominal	45	10	06	
• Inguinal	49	10	04 08	
Hepatomegaly	20	05	02 03	
Splenomegaly	43	04	05 03	
Bone marrow infiltration	10	02	04 05	
Extra nodal site	GIT -06		CNS-02	GIT-01
CNS-04		Breast-01		
Breast-02		Pericardium		
Tonsil-02		-01		
Para nasal sinus -02		Pleura-02		
Para nasal sinus -01				
Shoulder Joint -01Leg -01				
AIHA	02		02	
ITP 02	01	—	02	
S LDH				
• Raised	23	10	11 03	
• Normal	20	06	— 09	
• Not documented	17		03 02	
ECOG·	d”2	4218	06100410	1103
• >2				
Staging ·	e”III/IV	45	10 13	09
• ≤II	15	06	01 05	

Table-2

HL and NHL distribution according to Immunohistochemistry n=226

B cell NHL=97	Number (%)	T cell NHL=28	Number (%)
DLBCL	60 (48%)	PTCL	16(12.8%)
· GCB	25	· PTCL NOS	13
· Non GCB	04	· Angioimmunoblastic	02
· Unclassifiable	03	· Anaplastic ALK neg	01
· Not documented	28	·	
FL(Follicular Lymphoma)	14(11.2%)	T Lymphoblastic	12(9.6%)
MZL(Marginal Zone Lymphoma)	07(5.6%)	Lymphoma	
CLL/SLL(Chronic Lymphocytic	04(3.2%	Hodgkins Lymphoma	66
Leukemia/ Small Lymphocytic		· Mixed cellularity cHL	24(36.36%)
Lymphoma)			
· Nodular sclerosis cHL	05(7.5%)		
PBL(Plasmablastic Lymphoma)	03(2.4%)	· Lymphocyte depleted	
MCL(Mantle cell Lymphoma)	03(2.4%)	· cHL	02
Burkitts L	03(2.4%)	· NLPHL	03
B LBL (B Lymphoblastic Lymphoma)	02(1.6%)	· Histopath+IHC HL	32(48.48%)
but without subtype			
HCL(Hairy cell leukemia)	01(0.8%)	mentioned	
NHL by histopath and limited panel IHC	35		

diagnosis evident by morphology and or IHC. International prognostic index (IPI) score for DLBCL was variable having 27 (45%) had IPI score 2-3(intermediate) and 25(41.6%) had high IPI 4-5 score, 08(13%) had low IPI score 0-1. DLBCL cell of origin was detected as non GCB in 25(41%), GCB in 04(6%) and unclassifiable in 03(5%) cases according to Han's algorithm , although 48% cases were not been able to be classified due to lack of documentation of CD10, BCL6 and MUM1 markers.

PTCL patients had similar fashion of clinical features. Most patients of the very aggressive T lymphoblastic lymphoma (T LBL) had mediastinal involvement.

Different modalities of chemotherapies were received in various lymphoma according to disease status, stage and their financial ability.

Discussion:

Subtype distribution of lymphoma varies strikingly by geographic, demographic, etiologic, ethnic and environmental factors. The heterogeneity of the lymphoma depends on these factors and presentation differs in different subtype. In this study we present the patterns and distribution of lymphoma according to WHO classification in a tertiary hospital based data in Bangladesh.

According to the SEER data HL made up of 11% of all lymphomas[6] and nodular sclerosis HL are more frequent than mixed cellularity (70% Vs 25%) in western countries.[7,8] In our 21 months hospital based data showed that higher HL (29%) patients were enrolled among all lymphoma with predominantly (36.6%) mixed cellularity (MC) cHL followed by nodular sclerosis (NS) cHL only 7%. It is to be mentioned that in half of cases (48%) histologic subtype were not mentioned, but all those cases were being confirmed by IHC. In a large retrospective study of China found that 73.3% of MC-cHL had EBV.[9] Although EBV was not confirmed in all cases in our study but childhood EBV associated infection may have contribution in high frequency of MC CHL in Asian country. Another difference in demography of HL in our study that we did not find any bimodal age distribution which was found in Europe and North America. Japan also shows that a single peak age of HL in elderly people.[10] Nakatsuka and Aozasa have pointed out that the bimodal age curve might be formed by the different peak ages of the two main subtypes, MC-CHL (later years) and NS-CHL (young adults).[11]

NHL is one of the leading hematological malignancy in adult worldwide. The mean age in western and Asian

countries is between 50 to 60 years.[12,13] In our study we found an earlier median age at diagnosis 43(12-90) years for all NHL patients and M:F ratio is 3: 1 that is almost similar to western countries ratio.

In our study, B-cell lymphoma comprises 86.25% and remaining 13.75% were T-cell lymphomas very close to that of other studies in India[4] but differs that of a large study in China[9] that reported higher percentage (30.2%) of PTCL and NK cell lymphoma. Researchers has suggested that environmental factors including EBV infection as well as exposure to pesticides and chemical solvents were strongly associated with the higher frequency of T-cell NHL in China considering the agricultural area.[9,14]

According to clinical behavior most of the NHL in this current study were aggressive (65%), followed by indolent (21%) and very aggressive (14%). With regards to NHL subtype distribution, DLBCL continues to be the dominant histology comprising 30-35% of all NHL cases worldwide and this proportion has been stable over the years.[15] Similarly in our study the most common variant NHL found was DLBCL although the percentage is higher (48.38%) than other studies. Next common variety lymphoma were PTCL, followed by lymphoblastic lymphoma and follicular lymphoma. Other non-Hodgkins lymphomas found scattered were marginal zone lymphoma, mantle cell lymphoma, chronic lymphocytic leukemia/small lymphocytic lymphoma, hairy Cell leukemia, plasmablastic lymphoma and Burkitts lymphoma.

Similar result was observed in an Indian study where higher frequency of DLBCL (50.2%) was followed by follicular lymphoma (13.2%),[16] though our study had lower frequency of follicular type (11%). However, this trend of low frequency of follicular type (1.8%) was observed in Asian studies too.[13]

The gene expression profile (GEP) in research has classified the prognosis of DLBCL according to cell of origin. Based on Han's algorithm[17] in our study DLBCL cell of origin was detected as non GCB in 41% (25), GCB in 6% (04) & unclassifiable in 5% (03) cases, although 48% cases were not been able to be classified due to lack of proper immuno-histochemistry profile whereas much higher percentage (79%) non GCB DLBCL was reported in Chinese patients.[18]

Most of the DLBCL patients (70%) had lymph node enlargement in different site including cervical, axilla, abdominal and inguinal region. About 30% patients had extranodal disease with or without nodal involvement, comprising most common extranodal site was GIT and CNS and rare sites were breast, para nasal sinus, shoulder and testes. Very few of DLBCL(10%) had BM involvement at initial diagnosis. Two third of DLBCL presented with advanced stage and 86% having systemic B symptoms in our study comparatively higher than South India (23.9%) and Pakistan (36.7%).[19,20]

PTCL patients had similar fashion of clinical features. Patients with LBL had mostly mediastinum as extranodal site of involvement.

Staging PET scan is not routinely done at our center due to lack of financial support of patient group, staging CT scan is done in almost every cases.

HL and NHL patients are being treated in this center with various chemotherapy protocols according to their disease status, staging and prognosis. Autologous stem cell transplant is available for the relapse and refractory lymphoma patients who are chemo-sensisitive with salvage chemotherapy.

Limitation:

Our study has some limitations. This is a small scale study in a short period that might not represent the national data. The pathological reports were not reviewed due to lack of central reference lab and limited number of hematopathologist in our country . Immunohistochemistry (IHC) facilities are available only in very limited laboratories and sometimes the reports are not comprehensive to reach a diagnosis. There is lack of institutional policy of keeping medical records of patients, so detail clinical information of Hodgkins lymphoma was not included in this study. However this study is able to reflect the clinicopathologic pattern and distribution of lymphoma in a single center .

Conclusion

The Non Hodgkin Lymphoma is a common hematologic malignancy worldwide including Bangladesh. But there is scarcity of national data representing incidence, subtype and clinical spectrum of lymphoma that is necessary for proper management and better outcome . Although this is a small scale retrospective study, this can lead raising awareness of doing large scale national

data registry for lymphoma patients thus will be helpful to deliver standard of care treatment facilities to lymphoma patients as well as Autologous stem cell transplant for relapsed lymphoma.

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