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Original Article

Incidence and clinicohematological profile of lymphomas in Southern Punjab Pakistan

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Abstract

Background: Lymphomas are ranked as the sixth most common malignancy worldwide. Endorsing a significant impact on the health sector among the developing countries like Pakistan. The aim of the current study was to estimate the burden and clinicopathological features of lymphomas in one of the major referral centres in Southern Punjab Pakistan.

Methodology: A descriptive cross-sectional study was conducted at the Pathology department of Nishtar Medical University, Multan January 2016 to August 2019. A total of 75 patients both males and females of all age groups with diagnosed lymphoma were enrolled in the study. Diagnosis was made on morphology and immunohistochemistry of lymph node and cases with complete immunohistochemical workup were included and those without immunohistochemical panel were excluded from the study. Baseline tests were performed and bone marrow specimens were extracted from all cases. The data was analyzed using SPSS Version 23.0.

Results: Out of the total, 22.6% patients had Hodgkin lymphoma (HL) and 77.4% had Non-Hodgkin lymphoma (NHL). Classical Hodgkin lymphoma (CHL) was the most frequent histology (94%) among HL patients while Diffuse large B cell lymphoma (DLBCL) was the commonest B cell NHL (29.3%) and T cell lymphoblastic lymphoma (T-LBL) was found to be the most common T cell variant (5.3%). B symptoms, splenomegaly and hepatomegaly were documented in 96%, 42.7% and 25.3% patients respectively. Moreover, the disease was nodal in 65% cases and extranodal presentation was observed in 35% of the cases. Cervical node (lymph node) was involved in 25.3% of the cases while bone marrow was involved in 53.3% cases. The patterns of bone marrow infiltration were para trabecular (24.3%), diffuse (22.5%), interstitial (1.8%) and mixed pattern (3.75%).

Conclusion: Lymphomas are relatively more common among younger population in Pakistan. NHLs constitute more than 2/3rd of all lymphomas with DLBCL as the commonest histology. Stage IV disease as evidenced by bone marrow infiltration is seen in more than half of our patients.

Keywords

Hodgkin Lymphoma, Non-Hodgkin Lymphoma, Splenomegaly, Hepatomegaly, Southern Punjab.

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Introduction

Lymphomas are a heterogenous group of clonal malignancies of lymphoid system[1]. The clinical spectrum is varied and signs and symptoms of chronic diseases such as tuberculosis (TB) and systemic lupus erythematosus (SLE) overlap. The earliest presentation of lymphoma is painless enlarged lymph nodes and fever for more than 3 days. Diagnosis is established on the basis of histopathological findings of affected lymph node. Viral infections such as human immunodeficiency viruses (HIV), Epstein–Barr virus (EBV), hepatitis C virus (HCV) and human T-lymphotropic virus (HTLV) are believed to be risk factors for the development of lymphoma[2,3].

Lymphomas can be broadly classified as HL and NHL[4] and high prevalence of the disease has been reported in the regions including Southwest Asia, Middle East and North Africa[5], comprises Pakistan as well and collectively called as Lymphoma belt. HL is reportedly the seventh most common tumor in Pakistan and ranks second among the pediatric population[6] while NHL is the fourth most frequently diagnosed and fifth leading cause of cancer death in Pakistan[7].

The aggressiveness of malignant tumors is influenced by a number of factors including cellular type, pattern, genetic mutation and host immune status[8]. Histopathology is the cornerstone to determine cell type with intricate details of cell size and nuclear configuration[9]. The pattern of infiltration of lymph nodes predicts clinical behaviour of lymphoma and is used to predict prognosis where diffuse growth pattern confers a worse prognosis than a follicular pattern[8]. Bone marrow biopsy is invaluable for staging purposes where its involvement represents stage IV disease and hence aggressive treatment plan[8]. Similarly, histological subtyping and bone marrow examination of Hodgkin's lymphoma also reflects upon prognostic characterization[8].

Variation in incidence of HL and NHL among different countries and within different regions of the same country has been reported in literature[9,10,11]. Pakistan has yet to develop its cancer registry, a couple of studies have been conducted in other regions of the country but the data from southern Punjab is lacking[1,5,6]. In a country like Pakistan with unequal healthcare facilities, the findings of one region cannot be generalized over other areas. This prompts the need to conduct a study specific to Southern Punjab to generate local data specifying this region only. Our aim was to explore the clinical presentation and hematological parameters of lymphoma among patients presenting at the biggest referral setup of Southern Punjab.

Methodology

In this descriptive cross-sectional study, a total of 75 patients with diagnosed lymphoma on the basis of morphology and immunohistochemistry were recruited from the Pathology department of Nishtar Medical University, Multan during January 2016 to August 2019. Anonymity of data was ensured and approval for evaluation of retrospective records was taken from the institutional review board. Records were evaluated for the patient's age, gender and clinical signs & symptoms.

Diagnostic tests for lymphoma including fine needle aspiration cytology (FNAC), excisional biopsy, immunohistochemistry and bone marrow testing was performed. Moreover, baseline laboratory examinations such as complete blood count (CBC), erythrocyte sedimentation rate (ESR), serum electrolytes, liver function tests (LFT), renal function tests, hepatitis B & C, lactic acid dehydrogenase (LDH), serum albumin and urine analysis along with radiological imaging was also performed. The immunohistochemistry panel included CD20, CD3, CD5, CD23, CD7,

CD45, Tdt, CD15, CD30, CD10, CD56, CD38, and CD138. The data was analyzed using SPSS Version 23.0, all quantitative variables were expressed as mean and standard deviation (SD) while frequencies and percentages were used for all qualitative variables. Chi-square test was applied for categorical variables where p-value < 0.05 was considered significant.

Results

A total of 75 patients were enrolled in the study, of them 73.3% were males and 26.7% were females with a mean age of 40.56±18.7 years. Clinicopathological characteristics of study population are presented in table I. Fever (45.3%) was the major symptom observed followed by weight loss and splenomegaly (42.7%). Cervical (25.3%) and Para aortic (22.6%) lymph nodes were the most frequent findings among the patients.

Table I: Clinicopathological characteristics of study population

Characteristic		n=75
Mean Age (Years)		40.56±18.7
Gender	Male	55(73.3)
	Female	20(26.7)
Age Groups	10-30	23(30.7)
	31-60	46(61.3)
	≥61	06(8.0)
Symptoms at presentation	Fever	34(45.3)
	Weight loss	32(42.7)
	Bleeding manifestations	14(18.7)
	Night sweats	06(8.0)
	Splenomegaly	32(42.7)
	Hepatomegaly	19(25.3)
Lymph Node	Cervical	19(25.3)
	Para aortic	17(22.6)
	Inguinal	10(13.3)
	Iliac and para iliac	08(10.6)
	Axillary	04(5.3)
	Generalized lymphadenopathy	05(6.6)
	Mediastinal	02(2.7)

*Values are given as mean ± SD or n(%)

Among HL, CHL was the most common i.e. found in 21.3% while in NHL, DLBCL was commonly observed (29.3%) followed by CLL (13.3%).

Table 2: Distribution of Hodgkin & Non-Hodgkin Lymphomas

Lymphomas	Subtypes	n(%)
HL	CHL	16(21.3)
	NLPHL	1(1.3)
NHL	DLBCL	22(29.3)
	CLL	10(13.3)
	FL	4(5.3)

T-LBL	4(5.3)
ALCL	3(4)
B-LBL	2(2.7)
MALToma	2(2.7)
MCL	2(2.7)
SLL	2(2.7)
PCM	2(2.7)
T-cell NHL	1(1.3)
MBL	1(1.3)
SMZL	1(1.3)
HCL	1(1.3)
THRBCL	1(1.3)

*CHL-Classical Hodgkin lymphoma; NLPHL-Nodular lymphocyte predominant Hodgkin lymphoma; DLBCL-Diffuse large B cell lymphoma; CLL-Chronic lymphocytic leukemia; FL-Follicular lymphoma; T-LBL-T lymphoblastic lymphoma; ALCL-Anaplastic large T cell lymphoma; B-LBL-B lymphoblastic lymphoma; MALToma-MALT lymphoma; MCL-Mantle cell lymphoma; SLL-Small lymphocytic lymphoma; PCM-Plasma cell myeloma; T-cell NHL-T-cell Non-Hodgkin Lymphoma; MBL-Monoclonal B lymphocytosis (MBL); SMZL-Splenic marginal zone lymphoma; HCL-Hairy cell leukemia; THRBCL-T cell/histiocyte rich large B cell lymphoma.

Mean Hb was 10.6g/dL, mean TLC 9.6 x 109/L, mean platelet count 315 x 109/L in HL patients. While in NHL, mean Hb was 10.8g/dL, mean TLC 20.67 x 109/L and mean Platelet count 290 x 109/L. The difference in mean values of Hb, TLC and platelet count between HL and NHL was statistically significant (P value <0.05).

Table 2: Clinical findings of the patients of both groups

Clinical Findings	HL (n=17)	NHL (n=58)
Mean Hb (g/dL)	10.6	10.8
Mean TLC x 109/L	9.6	20.67
Mean PLT x 109/L	315	290
Mean LDH IU/L	400.3	475
Observed Deficiencies n(%)		
Anemia		18(24)
Leucopenia		8(10.7)
Thrombocytopenia		13(17.3)
Bicytopenia		4(5.3)
Pancytopenia		5(6.7)
Leukocytopenia		25(33.3)

*Values are given as Mean & n(%)

*Hb- Hemoglobin; TLC-Total Leucocyte Count; PLT-Platelet; LDH-Lactate Dehydrogenase

Total 8.0% and 14.7% of our patients were seropositive for HBsAg and anti HCV respectively. HBsAg positivity was seen only in NHLs while anti HCV was seen in both types of lymphomas. None of the results however achieved statistical significance. 10.34% of indolent and 6.8% of aggressive lymphomas showed HBsAg positivity. While anti HCV was positive in 1.72% of indolent

and 8.6% of aggressive lymphomas. Bone marrow infiltration was present in 53.3%. The most common patterns of bone marrow infiltration in NHL were paratrabecular (24.3%), diffuse (22.5%), interstitial (1.8%) and mixed (3.75%).

Table 3: HBsAg and anti HCV positivity in Hodgkin and Non-Hodgkin lymphomas

Diagnosis		Anti HCV positivity	p-value	HBsAg positivity	p-value
HL	CHL	1(6.25)	0.439	-	-
NHL	DLBCL	4(18)	0.721	3(13.6)	0.351
	CLL	2(20)	0.635	1(10)	1.000
	FL	2(50)	0.100	-	-
	T-LBL	-	-	1(25)	0.289
	BLBL	-	-	1(50)	0.155
	MALToma	1(50)	0.274	-	-
	MBL	1(100)	0.147	-	-

*HL-Hodgkin Lymphoma; NHL-Non-Hodgkin Lymphoma; HCV-hepatitis C virus; HBsAg-Hepatitis B surface antigen; DLBCL- Diffuse large B cell lymphoma; CLL-Chronic lymphocytic leukemia; FL-Follicular lymphoma; T-LBL-lymphoblastic lymphoma; BLBL-B lymphoblastic lymphoma; MALToma-MALT lymphoma; MBL-Monoclonal B lymphocytosis; CHL-Classical Hodgkin lymphoma

Discussion

The study results indicate that HL was prevalent among 22.6% of the study population while NHLs were found in 77.4% patients presented to the study setting. Among NHL, B cell NHL constituted 85% and T cell NHL was common in 15% which is consistent with another Pakistani study conducted at Ziauddin hospital (87% B cell type and 13% T cell type)[12]. Moreover, the percentage of histological characteristics of NHLs in western population is also similar to our results[13]. Although our results are similar to an Indian study with respect to B cell lymphoma[11] but for T cell lymphomas, there are geographical variations reported with ALCL as the most frequent T cell variant in Northeast India[9] and TLBL in other regions of India[14]. Overall, DLBCL, CLL, FL and TLBL constituted majority of NHLs in our study (Table 2).

Mean age in our study is lower than that in a Northeast Indian study which included 54 years of patients but similar to a West Indian study having 39.9 years as the mean age of the lymphoma patients[9]. The age range was wide (10-75 years) and there was a preponderance of younger people in our study with only 8% being older than 61 years. The results are comparable to other Southeast Asian countries[15,16] but different from the data provided by United States of America (USA)[10]. Possibly shorter life expectancy and relatively younger population in developing countries might be one explanation of this disparity[17]. Moreover, B symptoms were observed among 96% of our patients which was different from study conducted by Sultan et al., where B symptoms were common among 80.4% patients[18]. The difference might be due to the fact that they included only NHLs in their study while we studied both Hodgkin and NHLs. The pattern of lymph node involvement in our study is similar to a European study by Krol et al., with cervical lymph node as the most common site (25.3%) and inguinal nodes being the least (13.3%)[19]. Our results are different from a local study by

Hingorjo et al., where para aortic nodes were most commonly involved[20].

Extranodal disease was seen in 35% of our patients at presentation. This is comparatively lower to 42.6% in Indian population[21]. Our HL patients had splenomegaly in 25% and hepatomegaly in 31.5%. A study from Liaqat National hospital has reported similar frequency of splenomegaly (25.8%) and lower frequency of hepatomegaly (17.7%)[22]. On the other hand, 75% and 68.4% of our patients with NHL had splenic and hepatic enlargement respectively. Our findings are comparable to a study conducted in Lahore i.e. it was similar for splenomegaly (76.67%) but different for hepatomegaly (46.67%)[23].

Anemia was present in 24% of our patients compared to 46% in an Indian study[9]. Our results indicate that seropositivity for HBsAg was more common in indolent lymphomas and anti HCV positivity was more frequent in aggressive lymphomas. While in Chinese population, both HBsAg and anti HCV were more commonly seen in indolent lymphomas[24]. The most common pattern of bone marrow infiltration in our patients of NHL was paratrabecular followed by diffuse, mixed and interstitial pattern of infiltration. This is in contrast with another study from Karachi, which has reported diffuse infiltration as the commonest pattern[25]. Our findings of most common pattern of bone marrow infiltration correspond with western statistics[26].

Conclusion

NHL is more common than HL in our study setup, NHL constituted more than 2/3rd of all lymphomas in our population. CHL was the commonest subtype of HL while DLBCL is the most frequent subtype of NHL. Our patients presented with lymphomas were with relatively younger age as compared to the western population. Stage IV disease as manifested by bone marrow infiltration was seen in more than half of the patients and the most common pattern of infiltration was paratrabecular.

Conflicts of Interest

None.

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