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Original Article

Type & Frequency of Lymphomas: Single Institution Experience

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ABSTRACT

Objective: To see the type and frequency of lymphomas.
Study Design: Prospective longitudinal study.
Place and Duration of Study: Department of Medical Oncology at Jinnah Postgraduate Medical Centre, Karachi from Jan 2019 to Dec 2019.
Methodology: Total of 150 patients with histopathological diagnoses of lymphoma of 17 to 71 years of age of either gender were included in the study using non-probability consecutive sampling technique. Prior to initiation of study ethics review committee has approved the study (NO.F.2-81-IRB/2019-GENL/10261/JPMC). The data regarding lymphoma type, histology, stage of disease, site, involvement of bone marrow, presence of B-symptoms were recorded.
Results: Majority of the patients were male i.e., (n=104, 69.3%) with the mean age of 45.29±17.76 years. Non-Hodgkin's Lymphoma presented as the most common type of lymphoma i.e., (n=107, 71.3%) whereas Hodgkin's lymphoma (HL) contributed for (n=43, 28.7%) cases. Assessment of clinicopathological features of lymphomas revealed that (n=58, 38.7%) cases had bone marrow involvement. B-symptoms appeared in (n=102, 68%) cases, (n=61, 40.7%) cases were stage IV and the most common site were Neck lymph nodes (n=82, 58.3%), followed by abdomen (n=20, 13.3%). There was statistically significant difference between type of lymphoma with respect to age (p=0.001) and gender(p=0.015)
Conclusion: Among lymphomas the most common type of lymphoma was Non-Hodgkin's Lymphoma, most common in patients >45 years of age showing relationship of its occurence with age and DLBCL is major subtype and among Hodgkin's lymphoma Classical type is the predominant type Epidemiologic characteristics and distribution of the disease varies with geographical region, racial & environmental factors.

Keywords: Carcinoma, epidemiology, Hodgkin's lymphoma, Histology, Lymphoma subtypes, Non- Hodgkin's lymphoma.

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INTRODUCTION

Lymphomas are distinct malignant tumors located in lymphoid tissues accounted for 4% of cancer globally and classified into Hodgkin's lymphoma (HL) and Non-Hodgkin's lymphoma (NHL).[1] Both of them arise by immune cells like T-cells, B-cells and NK-cells and displays different behavioral, prognostic and epidemiological characteristics and their response to treatment. In US for 2019, about 3540 women & 4570 men were diagnosed with HL, whereas 33,110 women & 41,090 men were diagnosed with NHL, affecting both children and adults .[2]

HL is rare and curable cancer and its occurring rate varies with geography, age and socioeconomic status. In Western countries its incidence is reported as 20-45% of malignant tumors whereas in Asian countries comparatively low incidence has been reported as 4.4-18%.[3] According to cancer report by Shaukat Khanum in Pakistan, Hodgkin's lymphoma is the 7th leading cancer (4%) and frequent among the age group less than and equal to 18 years .[4]

Non-Hodgkin's lymphoma is a lymphoproliferative disorders, rising from lymph nodes with heterogeneous, histological and clinical characteristics.[5] The occurrence rate of NHL is rising in many regions. In Scotland, England & Wales the age-adjusted incidence has raised by 35% in 30 years .[6,7] Relatively comparable pattern has been found in India, Brazil, Japan, Western Europe and Singapore.[8] While in Pakistan NHL is one of the common cancer.[9] As the incidence of lymphoid malignancies is rising globally day by day with marked variations across geographic regions & socioeconomic factors and there is scarce data available in Pakistani population. International data isn't applicable in our population because it varies due to geographical area, environmental factors and genetic makeup. Therefore in this study we have observed the frequency of lymphoma with demographic & clinical findings in patients presenting at tertiary care hospital.

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METHODOLOGY

The prospective longitudinal study conducted at the Oncology Department, Jinnah Postgraduate Medical Center (JPMC), which is considered as one of the biggest government-operated hospitals in Karachi. The sample size was calculated by using Open Epi online sample size calculator, based on frequency of Hodgkin's lymphoma as 16.83% [10], margin of error as 5% and 95% confidence level. The estimated sample size came out as 150 patients. Non-probability consecutive sampling technique was employed.

Inclusion Criteria: All diagnosed cases of lymphoma of 17 to 71 years of age of either gender were included in the study.

Exclusion Criteria: The patients who had underwent chemotherapy were excluded from the study.

The study was conducted as per ICH-GCP guidelines, prior to initiation ethics review committee has approved the study (NO.F.2-81-IRB/2019-GENL/ 10261/JPMC) and informed consent was taken from all recruited pa-tients.

The subject's demographics, baseline characteristics, lymphoma subtype & clinicopathological features including Immunohistochemistry panel, bone marrow involvement, presence of B-symptoms, stage & site of the disease (using PET or CT scan with contrast) were assessed utilizing a predesigned proforma. For analysis of all the variables, SPSS version 23 was employed. In case of evaluation of quantitative variables Mean and SD were calculated whereas for qualitative variables frequency and percentage were determined. Chi-square test was applied for determination of significance between age and gender with type of lymphoma, *p*-value ≤0.05 was the criteria for statistical significance throughout the analysis.

RESULTS

Total of 150 patients were included in the study. Mean age of the patients was 45.29±17.76 years. The majority of the patients were males (n=104, 69.3%) whereas (n=46, 30.7% were females. Most common ethnicity was Sindhi (n=57, 38%) followed by Urdu speaking (n=51, 34%) as presented below in Table-I.

As summarized in Table-II, out of 150 cases of lymphoma, (n=107, 71.3%) cases were recognized as Non-Hodgkin lymphoma, whereas (n=41, 28.7%) cases as Hodgkin lymphoma. Among Hodgkin lymphoma subtypes, (n=43, 100% (28.7% of all hostologies) cases were classical Hodgkin's lymphoma (CHL). The mixed cellularity Hodgkin lymphoma was the frequent histology among Classical Hodgkin lymphoma (n=34, 79% of CHL (22.7% of all histologies). Among Non-Hodgkin lymphoma, (n=95, 88.8%) had B cells and (n=12, 11.2%) had T-cells. The diffuse large B-cell lymphoma (n=75, 80% of B-cells (50% of all histologies) was the frequent histology among B-Cell Non-Hodgkin lymphomas. whereas peripheral T-Cell lymphoma (n=8, 66.7% of T-cell and 5.4% of all histologies) were the most frequent histology among T-Cell Non-Hodgkin lymphomas.

Table-I: Demographics and Baseline Characteristics (n=150)

Variable	Mean±SD
Mean Age in years	45.29±17.76
Gender	n(%)
Male	104, 69.3%
Female	46, 30.7%
Ethnicity	
Sindhi	57, 38.0%
Urdu	51, 34.0%
Pashto	14, 9.3%
Balochi	13, 8.7%
Punjabi	11, 7.3%
Gujrati	2, 1.3%
Hindko	2, 1.3%

Clinicopathological characteristics including bone marrow involvement, presence of B-symptoms, site and stage of lymphoma are presented in Table below.

Table-II: Distribution of Lymphoma Subtypes and Histological Categorization (n=150)

Types of Lymphoma	Subtypes	Histology	n(%)
Hodgkin's lymphoma (n=43, 28.7%)	Cassical Hodgkin's lymphoma (n=43, 100%) (28.75% of all lymphomas)	Mixed cellularity Hodgkin lymphoma	n=34, 22.7%
		Nodular sclrosing Hodgkin Lymphoma	n=6, 4.0%
		Unspecified	n=3, 2.05%
	Non-classical Hodgkin's lymphoma (n=0)	-	-
Non-Hodgkin's lymphoma (n=107, 71.3%)	B-cells (n=95, 88.8%) (63.3% of all lymphomas)	Diffuse large B-cell lymphoma (DLBCL)	75, 50.0%
		Follicular lymphoma	n=11, 7.3%
		Burkitt lymphoma	n=3, 2.0%
		Mantle cell lymphoma	n=3, 2.0%
		Marginal Zone Lymphoma	n=3, 2.0%
	T-cells (n=12, 11.2%) (8% of all lymphomas)	Peripheral T-Cell Lymphoma	n=8, 5.4%
		Extranodal NK/T-cell lymphoma	n=3, 2.0%
		Adult T-cell leukemia/lymphma	n=1, 0.6%

The (n=58, 38.7%) cases had bone marrow involvement. Of all cases (n=102, 68%) of the cases had B-symptoms, (n=61, 40.7%) had stage of tumor as IV. The Neck lymph nodes (n=82, 58.3%) were the most frequent anatomical site, followed by abdomen (n=20, 13.3%), mediastinum (n=9, 6%) and other sites as depicted in Table-III respectively.

Stratification of lymphoma types with respect to age and gender was shown in Table-IV. There was statistically significant difference found between type of lymphoma with respect to age (p<0.001) and gender (p<0.015).

Table-III: Clinicopathological Features of Lymphoma (n=150)

Variables		Number of Patients (n), n(%)
Bone marrow involved	No	92, 61.3%
	Yes	58, 38.7%
B-symptoms	Present	102, 68.0%
	Absent	48, 32.0%
Stage	1	26, 17.3%
	2	26, 17.3%
	3	37, 24.7%
	4	61, 40.7%
Site	Neck Lymph Nodes	82, 58.3%
	Abdomen	20, 13.3%
	Bone	12, 8.0%
	Mediastinum	9, 6.0%
	Skin	2, 1.3%
	Liver	5, 3.3%
	Nasopharynx	4, 2.7%
	Testis	2, 1.3%
	Chest	5, 3.3%
	Spleen	2, 1.3%
	CNS	2, 1.3%
	Colon	1, 0.7%

Table-IV: Stratification of Lymphoma (n=150)

Variables	Type of Lymphoma		Total (n), n(%)	p-value
	Non-Hodgkin's Lymphoma	Hodgkin's Lymphoma		
Age groups				
≤17 years	-	6	6, 4%	0.001
18-30 years	13	13	26, 17.3%	
31-45 years	35	13	48, 32%	
≥46 years	59	11	70, 46.7%	
Gender				
Male	68	36	104, 69.3%	0.015
Female	39	7	46, 30.7%	

DISCUSSION

Lymphocyte play very critical role in immune system when lymphocytes start growing in abnormal manner they transform into lymphomas which can happen in any age. Lymphomas accounts for 4% of all cancer globally and classified into two major types such as Hodgkin's lymphoma (HL) and Non-Hodgkin's lymphoma (NHL) 1. Pakistan is one of the country which is at "lymphoma belt" 1. In Asian countries HL incidence has been reported as 4.4-18% where as in Western countries comparatively high incidence is reported as 3(20-45%). However, in 30 years the age-adjusted incidence of NHL has raised by 35% in Scotland, England & Wales.[6,7] The aim of the present study was to evaluate the frequency lymphoma types, its demographical & clinical findings in patients presenting at tertiary care hospital.

Lymphoma is overall 4th most prevalent cancer in males with 6% occurrence. In the present study the average age of the patients with lymphoma was 45.29±17.76 years and majority of the patients belonged from age ≥45 years (n=70, 46.7%) with predominance of males (n=104, 69.3%). In study conducted in Pakistan by Nawaz *et al*. also showed that men are more influenced by lymphoma (74%) as compared to women (26%) and majority of them belonged to age ≥51 years.[11] Yakubu *et al*. conducted a study in North Eastern Nigeria which also revealed that lymphoma was frequent among males.[12] The incidence of lymphoma higher among older age might be due to presence of comorbidities and variation of pharmacokinetics by worse host tissue tolerance, microenvironment change with increasing age related to therapy, complications like cardiovascular issues and infections due to high exposure to treatment. However the molecular mechanism about the sexual difference is not clear yet.[13]

As this study was conducted at the tertiary care hospital of Karachi, Sindh therefore most of the patients were sindhi (n=57, 38%) followed by urdu speaking (n=51, 34%). South Asians populations such as Pakistani, Indians & Bangladeshis and Blacks such as Carribeans & Africans are wider ethnic groups with diverse lifestyles, environmental factors, ancestry and cultures therefore the incidence of lymphoma varies among them.[14]

Literature reviews have shown NHL in United States was 4.3%.[15] Worldwide 50% cases were diagnosed with NHL specifically in western population like Australia and North America.[16,17] In the present study, the proportion of NHL (n=107, 71.3%) is higher as compared to HL (n=43, 28.7%). Shahid *et al*. conducted a similar study at Karachi among 318 consecutive patients of lymphoma out of which 25% were HL and 75% were NHL.[18] Sharma *et al*. also found the similar results, 39% were HL & 61% were NHL.[19]

Study by Lee *et al.* revealed histopathological features for diagnosis of HL and presence of multinucleated giant neoplastic cell and Reed-Sternberg cells on CD15 and CD30 are diagnostic factor for classic HL Tests 3. It usually affects adult and older people >55 years old. Study by Carballo-Zarate, *et al.* reported the four subtypes among which nodular lymphoma (47%) and mixed cellularity lymphoma (38%) cases are mostly present.[20] Furthermore, researches have investigated strong association between Epstein Barr virus (EBV) and HL. It is reported that EBV and mixed cellularity HL is strongly associated with each other while nodular HL is familial and has no positive correlation with EBV.[21] In the present study, (n=43, 28.7%) had classical Hodgkin's lymphoma (CHL) and among them (n=34, 79% (22.7% of all histopathologies) showed the mixed cellularity type Hodgkin lymphoma.

Different biological markers like CD20, CD79a, BCL6, CD10, MYC, BCL2, Ki67, IRF4, CyclinD1, CD5 and CD23 are suggestive of B-cell lymphoma are diffuse large B-cell lymphoma (DLBCL). Moreover, studies have found out its presence in usually adult population and yearly there are around 4 cases reported out of 100 thousand cases.[22] Other common type of NHL is Burkitt lymphoma that has prognostic biological marker *c-MYC*. Unlikely DBCL, it affects children.[23] In the present study, (n=95, 88.8% (63.3% of all histopathologies) had B cells and (n=12, 11.2% (8% of all histopathologies) had T-cells in NHL. The diffuse large B-cell lymphoma (n=75, 80% (50% of all histopathologies) was the frequent histology among B-cells whereas peripheral T-Cell lymphoma (n=8, 66.7% of T-cell (5.4% of all histopathologies) were the most frequent histology among T-cells.

The results of this study also showed that majority of the patients were presented with stage 4 (n=61, 40.7%) of disease followed by stage 3(n=37, 24.7%) & stage 1 & 2 (n=26, 17.3% each). In a previous study conducted by Faizan *et al*. compared the frequency of HL between Lahore & UK and found 90% of the patients had stage 3 or 4 of disease at Lahore whereas majority of the patients had stage 2 & 3 of disease at UK. This may be due to delay in diagnosis and low socio economic status.[24] In the present study (n=58, 38.7%) of the patients had bone marrow involvement, (n=102, 68%) had B-symptoms. The Neck lymph nodes (n=82, 58.3%) were the most frequent anatomical site, followed by abdomen (n=20, 13.3%), mediastinum (n=9, 6%). A Korean study which revealed 70% cases of extranodal lymphoma than 30.4% cases of nodal lymphomas and GI tract was the most frequent site.[25] As HL is a rare lymphoma, it mostly affects both younger and adult populace, however the incidence is more between ages of 15-49 years. Whereas NHL is a common tumor and diagnosis mostly in older age people.[1] In the present study, the frequency of lymphoma was high among age group ≥46 years (n=70, 46.6%). The frequency of Hodgkin's lymphoma & Non-Hodgkin lymphoma have also been observed as increasing with age and the relationship was statistically significant (p<0.05). As discussed, researchers have found that males are more likely to develop NHL and HL as compare to females 18. The similar findings have been observed in the present study between type of lymphoma and gender and the relationship was statistically significant (p<0.015).

Hence, this study reported burden of different types of lymphomas that reflect proper and early screening for this disease. Within the limitation of this study, further large sample size studies are recommended.

CONCLUSION

Pakistan's population is ethnically diverse with distinct ethnic groups inhabiting various parts of the country. The epidemiology of this disease is related to different racial and environmental factors. As per the results of this single institution experience, distribution and frequency of subtypes of malignant lymphomas is not unique at this center as compared to other countries of the region in which NHL is the most common subtype of lymphoma.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

SH: & GH: Data acquisition, data analysis, data interpretation, approval of the final version to be published.

SZ: & MH: Conception, study design, drafting the manuscript, approval of the final version to be published.

MN: & RB: Critical review, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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