ORIGINAL ARTICLE

Frequency of Different Types of Non-hodgkin Lymphoma and their Association with Demographics and Stage of Disease: An Institutional Perspective from Pakistan

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ABSTRACT

Introduction: Lymphoma is the fifth most common cancer and affects both genders throughout the world. The purpose of current study is to find out the frequency of different types of Non-hodgkin lymphoma and its association with age, gender and stage of disease in Pakistani population.

Methods: It was a retrospective study conducted at Department of Oncology, Liaquat National Hospital. The study included all patients with histopathological diagnosis of NHL that reported in adult oncology outpatient department from year 2005 to 2015. The pertinent clinical information and demographic data of all the patients were recorded.

Results: Total of 214 cases of NHL were reported between 2005 and 2015. Out of 214 patients, 113 (52.8%) were males and 101 (47.2%) were females. The mean age at diagnosis was 50.85 ± 15.64 years. Most of the cases were B cell lymphomas (n=189, 88.32%), had intermediate tumor grade (n=150, 74.61%) and stage 3 disease (n=55, 26.19%). Half of the cases had nodal presentation (n=114, 53.27%). Diffuse large B cell lymphoma was the most common type (n=140, 65.42%), followed by follicular lymphoma (n=17, 7.94%) while the most rare type was T lymphoblastic leukemia/lymphoma (n=3, 1.40%). Age (p<0.001), gender (p=0.001) and tumor grade (p<0.001) were significantly different among subtypes.

Conclusion: Non-hodgkin lymphoma has different presentations in different geographic locations which could be due to different environmental and lifestyle factors. In our study the male population was predominantly affected. Intermediate grade and nodal lymphomas were more frequent and the median age of presentation was lower than the rest of the world.

Keywords: Lymphoma, age, stage, gender, nodal, extra nodal, subtypes.

BACKGROUND

Lymphoma is the fifth most common cancer and affects both genders throughout the world. It can be categorized into two subtypes: non-hodgkin lymphoma (NHL) and hodgkin lymphoma (HL). Ann Arbor classification is used for the staging of lymphoma [1].

Being the 8th most commonly diagnosed cancer in men and the 11th most in women, NHL accounts for 5.1% of all cancer cases and 2.7% of all cancer deaths worldwide. There are about 30 different subtypes of NHL [2]. A large geographical disparity has been noted in the distribution of NHL types, with follicular and diffuse lymphoma being more frequent in North America and Europe, and T-cell lymphoma being more common in Asia [3, 4]. The median age of patients who are diagnosed with NHL varies according to the histologic subtype, although most subtypes increase exponentially with increasing age. Gradual increase in the annual incidence has been observed in our part of the world recently [5]. At national level, non-hodgkin lymphoma is the 4th commonest malignancy [6, 7].

In Pakistan, a huge increase has been seen in the incidence of lymphoma patients. Therefore, we should know the epidemiology of lymphoma in our population so it helps other health care professionals in a finer comprehension of risk factors, prognostic factors and the recent trends of lymphoma management. Therefore, the current study was conducted to find out the frequency of different types of NHL and its association with age, gender and stage of disease in Pakistani population.

METHODS

This was a retrospective study conducted at the Oncology Department of Liaquat National Hospital Karachi. The study included all patients with histopathological diagnosis of NHL that reported in oncology OPD from year 2005 to 2015. The pertinent clinical information and demographic data of all the patients were retrieved.

Staging was done using the Lugano modification of an arbor staging system by doing required investigations like radiological imagings such as CT scans and bone marrow or PET scans. Grading was done using the working formulation classification of Non-hodgkin lymphoma.

The collected data was entered into IBM SPSS version 20 for statistical analysis. Categorical variables were presented as frequency and percentage while continuous

variables were summarized in terms of mean ± standard deviation. Pearson Chi-square/Fisher-exact test was applied to assess the association of age, gender and disease stage with different types of Non-hodgkin lymphoma. P-value < 0.05 was considered statistically significant.

RESULTS

Total of 214 cases of NHL were reported between 2005 to 2015. Patients' clinical characteristics and demographic are shown in Table **1**. At diagnosis the mean age was 50.85 ± 15.64 yrs. Most of the patients presented with stage III disease (n=55, 26.19%). Out of 214 patients, 113 were male (52.8%) and 101 (47.2%) were female. The most common site of lymphoma was nodal (n=114, 53.0%) followed by both nodal and extranodal (n=49, 22.90%) and only extranodal involvement was seen in 47 (21.96%) of patients. Tumor stage, grade and nodal status were not known on 58 (27.10%), 17 (7.94%) and 4 (1.87%) cases respectively because these cases only visited once. Intermediate grade lymphoma comprised 150(70.1%) of NHL followed by low grade lymphoma (n= 2913.6%), then high grade lymphoma (n=18, 8.4%).

**Table 1:** Socio-demographic and Clinical Characteristics of Patients.

Patients' Characteristics	Frequency (%)
Age (in years)#	50.85 ± 15.64
Gender	
Male	113 (52.8)
Female	101 (47.2)
Tumor Grade	
Low	29 (14.72)
Intermediate	150 (76.14)
High	18 (9.13)
Presentation	
Nodal	114 (54.29)
Extranodal	47 (22.38)
Both nodal and extranodal	49 (23.33)
Tumor stage	
Stage I	22 (14.10)
Stage II	43 (20.48)
Stage III	55 (26.19)
Stage IV	36 (17.14)

#: age is expressed as mean ± standard deviation

B cell lymphomas were more frequent (n=189, 88.32%) whereas the frequency of T cell lymphoma was (n=25, 11.68%) (**Fig. 1**). Diffuse large B cell lymphoma was the most common type (n=140, 65.4%) followed by follicular lymphoma (n=17, 7.95 %.), anaplastic large cell lymphoma (n=11, 5.14), other B cell lymphomas (n=10, 4.67%), other T cell lymphoma (n=7, 3.27). Less frequent subtypes included CLL/small lymphocytic lymphoma (n=6, 2.8%), mantle lymphoma (n=6, 2.8%), marginal zone lymphoma (n=6, 2.8%), peripheral T cell lymphoma (n=4, 1.9%), Burkitt lymphoma (n=4, 1.9%). Only 3 (1.40%) patients had T lymphoblastic leukemia/ lymphoma (**Fig. 2**).
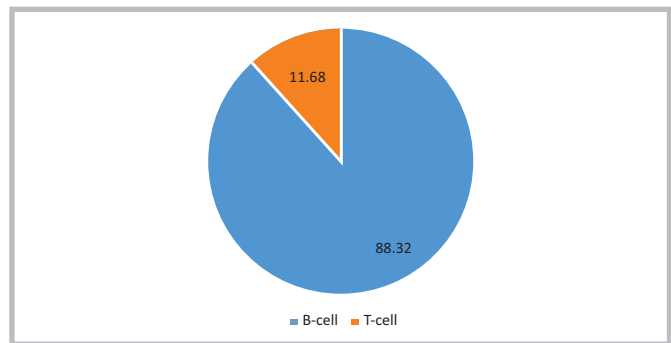
Fig. (1): Frequency of B cell and T cell lymphomas.
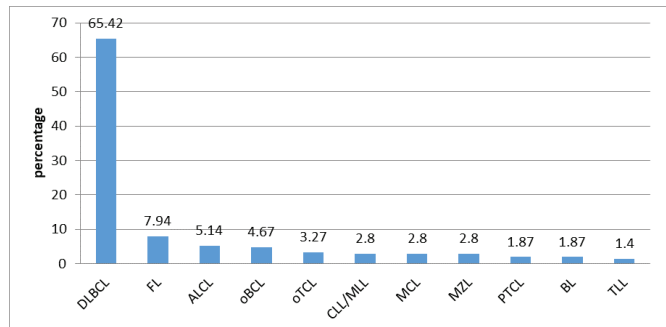
Fig. (2): Frequency of different types of non-hodgkin lymphoma.

DLBCL: Diffuse large B cell lymphoma, FL=Follicular lymphoma, ALCL=Anaplastic large cell lymphoma, oBCL=other B cell lymphoma, oTCL= other T cell lymphoma, CLL/SMLL=CLL/Smll lymphocytic lymphoma, MCL=Mantle cell lymphoma, MZL=Marginal zone lymphoma, PTCL=Peripheral T cell lymphoma, BL=Burkitt Lymphoma, TLL=T lymphoblastic leukemia/lymphoma.

Tumor stage (p=0.249) and presentation (p=0.484) was not significantly different among patients with different types of lymphoma. Age was significantly associated with sub-types of lymphoma (p<0.001). Among all age groups, proportion of patients with diffuse large B cell lymphoma was significantly higher as compared to other sub-types (Table **2**).

Gender was also significantly associated with NHL sub-types (p=0.001). Peripheral T cell lymphoma, burkitt's Lymphoma and mantle cell lymphoma was present in males only. Anaplastic large cell lymphoma, t cell lymphoma and T lymphoblstic lymphoma were higher in males in our sample as compared to females whereas proportion of female was higher among those who presented with diffuse large B cell lymphoma, follicular lymphoma, other B cell lymphoma, CLL lymphocytic lymphoma and marginal zone lymphoma.

DISCUSSION

In this retrospective study we studied the different types of Non-hodgkin lymphoma reported from 2005 to 2016 and the clinical relations of these types with stage and demographics to understand this diverse and challenging group of malignancy for proper treatment.

Analysis of our data reveals that most of our patients were males which is similar to the other studies conducted in

Table 2: Association of patients' characteristics with histological sub-types.

-	DLBCL n(%)	FL n(%)	ALCL n(%)	oBCL n(%)	oTCL n(%)	CLL/SMLL n(%)	MCL n(%)	MZL n(%)	PTCL n(%)	BL n(%)	TLL n(%)	P-value
Age groups												
<30 years	20(66.7)	0(0)	4(13.3)	0(0)	1(3.3)	0(0)	1(3.3)	0(0)	0(0)	3(10)	1(3.3)	
30-50 years	42(63.6)	6(9.1)	2(3)	1(1.5)	6(9.1)	2(3)	0(0)	2(3)	3(4.5)	0(0)	2(3)	**<0.001
>50 years	78(66.1)	11(9.3)	5(4.2)	9(7.6)	0(0)	4(3.4)	5(4.2)	4(3.4)	1(0.8)	1(0.8)	0(0)	
Gender												
Male	71(62.8)	4(3.5)	10(8.8)	4(3.5)	4(3.5)	2(1.8)	6(5.3)	2(1.8)	4(3.5)	4(3.5)	2(1.8)	**ł0.001
Female	69(68.3)	13(12.9)	1(1)	6(5.9)	3(3)	4(4)	0(0)	4(4)	0(0)	0(0)	1(1)	
Presentation												
Nodal	68(59.6)	11(9.6)	9(7.9)	5(4.4)	3(2.6)	5(4.4)	5(4.4)	2(1.8)	2(1.8)	2(1.8)	2(1.8)	
Extranodal	37(78.7)	1(2.1)	2(4.3)	1(2.1)	2(4.3)	0(0)	0(0)	2(4.3)	1(2.1)	1(2.1)	0(0)	ł0.484
Both nodal & extranodal	31(63.3)	5(10.2)	0(0)	4(8.2)	2(4.1)	1(2)	1(2)	2(4.1)	1(2)	1(2)	1(2)	
Tumor stage												
Stage I	17(77.3)	1(4.5)	2(9.1)	1(4.5)	1(4.5)	0(0)	0(0)	0(0)	0(0)	0(0)	0(0)	
Stage II	30(69.8)	0(0)	3(7)	0(0)	1(2.3)	1(2.3)	2(4.7)	3(7)	1(2.3)	1(2.3)	1(2.3)	ł 0.313
Stage III	35(63.6)	3(5.5)	2(3.6)	3(5.5)	3(5.5)	2(3.6)	1(1.8)	2(3.6)	0(0)	3(5.5)	1(1.8)	
Stage IV	18(0)	7(0)	1(0)	2(0)	1(0)	3(0)	1(0)	1(0)	2(0)	0(0)	0(0)	

DLBCL: Diffuse large B cell lymphoma, FL=Follicular lymphoma, ALCL=Anaplastic large cell lymphoma, oBCL=other B cell lymphoma, oTCL= other T cell lymphoma, CLL/SMLL=CLL/Smll lymphocytic lymphoma, MCL=Mantle cell lymphoma, MZL=Marginal zone lymphoma, PTCL=Peripheral T cell lymphoma, BL=Burkitt Lymphoma, TLL=T lymphoblastic leukemia/lymphoma.
**Signiﬁcnt at P<0.01 level, ł denotes Fisher exact test was applied.

Pakistan [8, 9] and in Asia and other parts of the world [10]. It could be due to the direct effect of estrogen on tumor cells or effect on anti-tumor response [11].

Non-hodgkin lymphoma is a disease of old age in North America and Europe. 60% of the patients are diagnosed at > 60 yrs. of age [12]. There is a difference in median age in different setups in our country [9]. The mean age in our population was 50 years which is similar in other Asian countries [13].

Non-hodgkin lymphoma involves the nodes as well as extra nodal organs like GI, head and neck and skin. Although in west the incidence of extranodal lymphoma is rising [10, 14] however, in our study nodal lymphoma is the predominant type where it consists of 53% of the cases and in other national studies as well [5, 15].

In our study we found that low grade lymphomas including follicular lymphomas and others account for 13% of the lymphoma which is similar in incidence to other parts of Asia [16-18]. However, in western countries such as USA it accounts for 25% to 30% of cases [19].

There is a great disparity in the geographical distribution of types of Non-hodgkin lymphoma with a higher amount of follicular and diffuse large B cell lymphoma in North America and Europe [4], and a higher amount of T-cell lymphoma in Asia [20]. However, the most familiar type of the Non-hodgkin lymphoma in our population was DLBCL which coincides with other studies done in Pakistan [6, 7, 21] and India [10] whereas in our study T cell lymphoma accounts for only 11.68%. We found high grade lymphomas in younger age and male gender which was also seen in other studies [20] whereas indolent lymphomas were usually present in females and in older age group [22].

CONCLUSION

Non-hodgkin lymphoma has different presentations in different geographic locations which could be due to different environmental and lifestyle factors.

In our study the male population was predominantly affected. Intermediate and nodal lymphomas were more frequent and the median age of presentation was lower than the rest of the world.

LIMITATIONS

The study includes patients from a single institution and may not be the true representative of population although the institution is a major health facility of the areas. Some of the patients only visited once so their grade, nodal status and subtype of lymphoma is not known.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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REFERENCES

1. Mumtaz T, Roohi N, Akhtar MW. Incidence and clinical manifestation of lymphoma in Central Punjab. Pak J Zool 2012; 44(5): 1367-72.

2. Loprinzi CL. Asco- sep medical oncology evaluation program. 4th ed. American Society of Clinical Oncology Inc; Alexandria, VA 2015.

3. Müller AMS, Ihorst G, Mertelsmann R, Engelhardt M. Epidemiology of non-hodgkin's lymphoma (NHL): trends, geographic distribution, and etiology. Ann Hematol 2005; 84(1): 1-12.

4. Boffeta P. Epidemiology of adult non-Hodgkin lymphoma. Ann Oncol 2011; 22(Supplement-4): iv27- iv31.

5. Nawaz MZ, Bilal M, Asgher M. Prevalence of lymphoma cancer in Punjab, Pakistan. Int J Appl Sci Biotechnol 2015; 3(2): 342-6.

6. Bukhari U, Jamal S, Lateef F. Non-hodgkin's lymphoma-a study. Pak Oral Dental J 2015; 35(3): 412-5.

7. Aziz Z, Rehman A, Akram M, Saeed A. Non-Hodgkin's lymphoma in Pakistan: a clinicopathological profile of 175 patients. J Pak Med Assoc 1999; 49(1): 11-5.

8. Naz E, Mirza T, Aziz S, Danish F, Siddiqui ST, Ali A. Frequency and clinicopathologic correlation of different types of Non-hodgkin's lymphoma according to WHO classification. J Pak Med Assoc 2011; 61(3): 260-3.

9. Ahmad M, Khan AH, Mansoor A. The pattern of malignant tumors in Northern Pakistan. J Pak Med Assoc 1991; 41(11): 270-3.

10. Smith A, Crouch S, Lax S, *et al.* Lymphoma incidence, survival and prevalence 2004-2014: sub-type analyses from the UK's Haematological Malignancy Research Network. Br J Cancer 2015; 112(9): 1575-84.

11. Horesh N, Horowitz NA. Does gender matter in non-hodgkin lymphoma? Differences in epidemiology, clinical behavior, and therapy. Rambam Maimonides Med J 2014; 5(4): e0038.

12. Weisenburger DD. Epidemiology of non-Hodgkin's lymphoma. Recent findings regarding an emerging epidemic. Ann Oncol 1994; 5(Suppl I): 19-24.

13. Nair R, Arora N, Mallath MK. Epidemiology of non-hodgkin's lymphoma in India. Oncology 2016; 91(suppl 1): 18-25.

14. Newell GR, Cabanillas FG, Hagemeiste FJ, Butler JJ. Incidence of lymphoma in the US classified by the working formulation. Cancer 1987; 59: 857-61.

15. Shabbir S, Ahmed KN, Marri M, *et al.* Epidemiological features of Lymphoma in Pakistan. Pure Appl Biol 2019; 8(1): 977-94.

16. Kinlen L. Immunosuppressive therapy and acquired immunological disorders. Cancer Res 1992; 52(19 Suppl): 5474s-76s.

17. Sandhu DS, Sharma A, Kumar L. Non-hodgkin's lymphoma in Northern India: an analysis of clinical features of 241 cases. Indian J Med Paediatr Oncol 2018; 39(1): 42-5.

18. Abdel-Fattah MM, Yassine OG. Non-hodgkin`s lymphomas in Alexandria, Egypt: incidence rates and trend study (1995-2004). Int J Cancer Res 2006, 2: 345-57.

19. Morton LM, Wang SS, Devesa SS, *et al.* Lymphoma incidence patterns by WHO subtype in the United States, 1992-2001. Blood 2006; 107: 265-75.

20. Burton C, Jack A, Adamson P, Roman E. Descriptive epidemiology. In Magrath IT, Eds. The lymphoid neoplasms. 3rd ed. London: Hodder Arnold 2010; pp. 47-58.

21. Pervez S. Non-hodgkin lymphoma (NHL) in Pakistan. Int J Mol Cell Med 2012; 1(1): 62-3.

22. Hellman S, Jaffe ES, DeVita Jr. VT. Hodgkin's disease. In: De Vita VT, Hellman S, Rosenberg SA, Eds. Cancer, principles and practice of oncology. 3rd ed. Philadelphia: Lippincott 1989, 1696-1740.