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.

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

# : 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).

**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.

<table>
<thead>
<tr>
<th>Tumor stage</th>
<th>DLBCL n(%)</th>
<th>FL n(%)</th>
<th>ALCCL n(%)</th>
<th>oBCL n(%)</th>
<th>oTCL n(%)</th>
<th>CLL/SMLL n(%)</th>
<th>MCL n(%)</th>
<th>MZL n(%)</th>
<th>PTCL n(%)</th>
<th>BL n(%)</th>
<th>TLL n(%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>17(77.3)</td>
<td>4(1.5)</td>
<td>2(9.1)</td>
<td>1(4.5)</td>
<td>1(4.5)</td>
<td>0(0)</td>
<td>0(0)</td>
<td>0(0)</td>
<td>0(0)</td>
<td>2(1.5)</td>
<td>1(2.5)</td>
<td>0.313</td>
</tr>
<tr>
<td>Stage II</td>
<td>30(69.8)</td>
<td>0(0)</td>
<td>3(7)</td>
<td>0(0)</td>
<td>1(2.3)</td>
<td>1(2.3)</td>
<td>2(4.7)</td>
<td>3(7)</td>
<td>1(2.3)</td>
<td>1(2.3)</td>
<td>1(2.3)</td>
<td>0.132</td>
</tr>
<tr>
<td>Stage III</td>
<td>35(63.6)</td>
<td>3(5.5)</td>
<td>2(3.6)</td>
<td>3(5.5)</td>
<td>2(3.6)</td>
<td>1(1.8)</td>
<td>2(3.6)</td>
<td>0(0)</td>
<td>3(5.5)</td>
<td>1(2.3)</td>
<td>1(2.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stage IV</td>
<td>18(73)</td>
<td>0(0)</td>
<td>0(0)</td>
<td>2(0)</td>
<td>1(2)</td>
<td>0(0)</td>
<td>1(2)</td>
<td>1(2)</td>
<td>0(0)</td>
<td>0(0)</td>
<td>0(0)</td>
<td>0.001</td>
</tr>
</tbody>
</table>


**Significnt at P<0.01 level, ƚ 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**