Evaluation of seasonality in the diagnosis of diffuse large B cell lymphoma in Turkey

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ABSTRACT

Introduction: Within subtypes of non-Hodgkin lymphoma (NHL), diffuse large B cell lymphoma (DLBCL) is most commonly diagnosed, with an incidence of 6/100,000 in Turkey (1,2). Most of the patients with DLBCL are over the age of 60 years, men are more frequently affected than women (3,4). Aetiology of DLBCL is unknown: several factors such as immunosuppression, AIDS, transplantation, autoimmunity, UV radiation, pesticides, hair dyes and dietary intake are hypothesized to be related with increased risk. Here, we aimed to determine the relationship between the diagnosis time of DLBCL and seasons.

Material and Method: A total of 369 DLBCL patients, diagnosed in our centre were included in the study. Data related to gender, age and time of diagnosis were analysed retrospectively.

Results: Median age of patients with DLBCL included in the study was 61 (range 16–81). The number of female patients were 178 (48.2%) and 191 (51.8%) were male. There was no relationship between the season of diagnosis time and DLBCL incidence (p:0.805).

Conclusion: According to our literature review, this is the first study that sort for a relationship between DLBCL diagnosis frequency and seasons in Turkey. We could not find a relationship between diagnosis time of DLBCL and seasons. This can be explained by the fact that the diagnosis of DLBCL displays a homogeneous distribution throughout the year due to a number of factors playing roles in the ethiopathogenesis of DLBCL.

Keywords: Non-Hodgkin lymphoma, diffuse large B cell lymphoma, seasonality

INTRODUCTION

Within subtypes of non-Hodgkin lymphoma (NHL), diffuse large B cell lymphoma (DLBCL) is most commonly diagnosed, with an incidence of 6/100,000 in Turkey (1,2). Most of the patients with DLBCL are over the age of 60 years, men are more frequently affected than women (3,4). Aetiology of DLBCL is unknown: several factors such as immunosuppression, AIDS, transplantation, autoimmunity, UV radiation, pesticides, hair dyes and dietary intake are hypothesized to be related with increased risk (5). Primary central nervous system lymphoma is highly associated with Epstein-Barr virus (EBV) (6). Vitamin D has an important role in immune system functioning and can act as an anti-proliferative in various haematological cancers (7,8). Other factors associated with sunlight exposure may also reduce prostate cancer and NHL risk. Sunlight exposure modulates subclinical both local and systemic inflammation on a cellular basis (12). Serum levels of the vitamin D is season dependant, dietary intake and vacations in sunny regions are main factors (13-15). Turkey is located between 36°–42° North parallels and 26°–45° East meridians. Months between December to February are winter; March to May are spring, June to August are summer and September to November are the autumn months (16,17).
Although several studies aimed to show the effect of between sunlight and lymphoma or solid tumours; data regarding seasonal variation of DLBCL diagnosis is scarce (18-20). Since vitamin D modulates proliferation and differentiation of cancer cells, we aimed to determine the relationship between the diagnosis time of DLBCL and seasons.

MATERIAL AND METHOD

The study was approved by Health Sciences University, Ankara Dr. Abdurrahman Yurtaslan Oncology Training and Research Hospital, Clinical Researches Ethics Committee (decision no: 2020-06/677; date: 24.06.2020). All procedures were performed adhered to the ethical rules and the Helsinki Declaration of Principles.

A total of 369 DLBCL patients, diagnosed in our centre were included in the study. Data related to gender, age and time of diagnosis were analysed retrospectively. Patients over 18 years of age who were diagnosed with DLBCL by examining tissue biopsy by immune histochemical analysis were included in the study. Patients who were diagnosed in another centre or those whose diagnosis date could not be reached were not included in the study.

Data analysis was performed using IBM SPSS v26 software. Descriptive statistics were utilized to summarize data. Categorical data were presented as number-percentages, and numerical data were presented as median, minimum, and maximum. Differences between categorical variables were analysed with Chi-Square tests. A p value of ≤0.05 was considered statistically significant. The study was approved by the local ethics committee.

RESULTS

Median age of patients with DLBCL included in the study was 61 (range 16–81). The number of female patients were 178 (48.2%) and 191 (51.8%) were male. The months when patients were diagnosed with DLBCL are shown in Table 1, and seasons are shown in Table 2. There was no relationship between the season of diagnosis time and DLBCL incidence (p=0.805).

DISCUSSION

In the majority of patients, the aetiology of DLBCL is unknown. Analysing seasonal differences of incidence can improve understanding of pathogenesis and risk factors of different diseases. Hodgkin’s disease and Burkitt’s lymphoma have been associated with EBV. Because of this infectious aetiology, researchers investigated to find out the relationship between the diagnosis time and seasons (21,22). Some previous reports have shown significant seasonal differences in Burkitt’s lymphoma diagnosis, based on the time of the first symptom (23-25). However, other studies have found no relation between seasons and Hodgkin’s disease and Burkitt’s lymphoma. In addition, other previous studies have reported Burkitt’s lymphoma endemicity to coincide with rainfall, low altitude, as well as malaria endemicity (26-30). It has been postulated that an increase in the incidence of Burkitt’s lymphoma seen during the rainy seasons may be due to increased mosquitoes that breed during the season, yet they are vectors for EBV. Furthermore, the rainy seasons also come with an increase in malaria infections, which is suspected to compromise the immunity, leading to increased susceptibility to Burkitt’s lymphoma (31,32). Williams et al. (33) and Oguonu et al. (34) reported a higher but not statistically significant difference in prevalence of Burkitt’s lymphoma in the dry season as compared to the wet season, in Uganda and Nigeria, respectively. Researchers had previously observed a significantly higher occurrence of Burkitt’s lymphoma in the wet season as compared to the dry one in South Africa and Malawi, respectively (32,35). Similarly, a seasonal variation is demonstrated in HL; a peak around March and a drop around September in the northern hemisphere is observed (36). Moreover, Porojnicu

Table 1. The distribution of diffuse large B cell lymphoma diagnosis times

<table>
<thead>
<tr>
<th>Months</th>
<th>DLBCL (n, %)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>January</td>
<td>24 (6.5%)</td>
<td></td>
</tr>
<tr>
<td>February</td>
<td>23 (6.2%)</td>
<td></td>
</tr>
<tr>
<td>March</td>
<td>40 (10.8%)</td>
<td></td>
</tr>
<tr>
<td>April</td>
<td>26 (7%)</td>
<td></td>
</tr>
<tr>
<td>May</td>
<td>30 (8.1%)</td>
<td></td>
</tr>
<tr>
<td>June</td>
<td>29 (7.8%)</td>
<td></td>
</tr>
<tr>
<td>July</td>
<td>34 (9.2%)</td>
<td></td>
</tr>
<tr>
<td>August</td>
<td>28 (7.6%)</td>
<td>p=0.337</td>
</tr>
<tr>
<td>September</td>
<td>26 (7%)</td>
<td></td>
</tr>
<tr>
<td>October</td>
<td>32 (8.6 %)</td>
<td></td>
</tr>
<tr>
<td>November</td>
<td>39 (10.5%)</td>
<td></td>
</tr>
<tr>
<td>December</td>
<td>38 (10.5%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>369 (100%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. The distribution of diffuse large B cell lymphoma diagnosis times

<table>
<thead>
<tr>
<th>Seasons</th>
<th>DLBCL (n, %)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Winter</td>
<td>85 (23.2%)</td>
<td></td>
</tr>
<tr>
<td>Spring</td>
<td>96 (25.9%)</td>
<td>p=0.805</td>
</tr>
<tr>
<td>Summer</td>
<td>91 (24.6%)</td>
<td></td>
</tr>
<tr>
<td>Autumn</td>
<td>97 (26.2%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>369 (100%)</td>
<td></td>
</tr>
</tbody>
</table>

DLBCL, diffuse large B cell lymphoma
et al. (37) defined season of diagnosis as a prognostic factor in HL, where a lower case fatality was observed during autumn, which may be due to a higher serum level of vitamin D. In a recent review by van der Rhee et al. (38) it was stated that epidemiological data suggests chronic but not intermittent sun exposure is associated with a reduced risk of colorectal, breast, prostate cancer and NHL, however, higher vitamin D levels were only associated with a reduced risk of colorectal and breast cancer. Low serum 25-hydroxyvitamin levels were not associated with the overall risk of lymphoma in two prospective studies (39,40); as well as Cohort Consortium Vitamin D Pooling Project of Rarer Cancer failed to show an elevated vitamin D level is associated with a reduced risk of NHL (41). Soni et al. (42) demonstrated an inverse association between sun exposure and risk of DLBCL. However, Swedish Lymphoma Register study failed to show a significant change in cases diagnosed per month (43). In our study, we could not demonstrate any significant seasonal variation of DLBCL diagnosis.

CONCLUSION

There are limited number of studies about the relationship between DLBCL and seasons. Among the studies examining this relationship in various geographical regions of the world, some studies found a relationship between lymphoma diagnosis frequency and seasons, whereas some other did not reveal such a relationship. According to our literature review, this is the first study that sort for a relationship between DLBCL diagnosis frequency and seasons in Turkey. We could not find a relationship between diagnosis time of DLBCL and seasons. This can be explained by the fact that the diagnosis of DLBCL displays a homogeneous distribution throughout the year due to a number of factors playing roles in the ethiopathogenesis of DLBCL.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was approved by Health Sciences University, Ankara Dr. Abdurrahman Yurtaslan Oncology Training and Research Hospital, Clinical Researches Ethics Committee (decision no: 2020-06/677; date: 24.06.2020).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES