Descriptive Epidemiology of Lymphoma in Northern Iran: Results from the Golestan Registry 2004–2013

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Abstract

Background: There is currently little known about the epidemiology of lymphomas in Iran. The aim of this paper is to describe the geographic and time variations in incidence rates of lymphomas in the Golestan province between 2004 and 2013.

Methods: The Golestan Population-based Cancer Registry (GPCR) routinely registers primary cancer patients from all sources (e.g. pathology centers, hospitals, etc.) throughout the Golestan province. We obtained data on newly-diagnosed lymphomas in Golestan during 2004-2013 from the GPCR dataset. Crude rates and age standardized incidence (ASR) rates (per 100 000) of lymphomas were estimated, jointpoint regression was used to quantify incidence trends and average annual percent changes (AAPCs) were calculated.

Results: In total, 898 new cases of lymphoma were registered in the GPCR during 2004-2013. The ASR of Hodgkin lymphoma (HL) was 1.5 and 1.1 in males and females, respectively, while corresponding non-Hodgkin lymphoma (NHL) rates were greater, at 6.5 and 3.4 in males and females, respectively. Our results indicated a significant difference in the trends of HL between males (AAPC = -3.2) and females (AAPC = 3.6, P value = 0.001). The incidence rates of lymphoma were considerably higher in the urban population (ASR = 7.3) compared to those residing in rural areas (ASR = 5.3, P value = 0.054). We also found higher incidence rates for both HL and NHL in the western parts of the Golestan province.

Conclusion: The incidence rates of lymphoma in the Golestan province are relatively high and vary geographically, with a higher incidence observed in the western area. Such differences may reflect unknown lifestyle and environmental determinants linked to ethnic susceptibility differing between the two areas.

Keywords: Epidemiology, Hodgkin Disease, Iran, Non-Hodgkin’s Lymphoma


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Introduction

With 509,590 and 79,990 cases respectively, non-Hodgkin lymphoma (NHL) and Hodgkin lymphoma (HL) are among the most common malignancies in the world, ranking 11th and 26th among the most frequent cancers.1 NHL is more common in more highly-resourced areas, and high incidence rates have been reported from Australia, and from selected countries in West and North Europe as well as North America. The rates are relatively low in most Asian and Eastern European countries.2 HL represents a heterogeneous group of malignant lymphoid neoplasms accounting for a significant proportion of cancers occurring in children, adolescents and young adults with two peaks occurring between the ages of 15 and 35 years, and after 50 years, whereas NHL generally occurs during adulthood and rarely in childhood, with a peak incidence between 5-9 years.3,4 Cancer has been reported as a major health-related issue in Iran. According to a recent report by the Ministry of Health in Iran, cancer has been suggested as the third most common cause of death after cardiovascular diseases and accidents.5 Based on the GLOBOCAN 2018 estimates, NHL and HL ranked as the 14th and 22nd most common cancers in Iran, respectively, with approximately 3000 NHL cases (3% of all cancers) and more than 1100 HL cases.6

The Golestan province, northern Iran, has been known as
Materials and Methods

In this cross-sectional study, we used data of primary incident cancer cases of lymphoma in the Golestan province over the diagnostic period 2004-2013, obtained from the GPCR. The details of the methods of data collection and data quality at the GPCR have been presented previously. Briefly, only primary cancers are registered, considering standard protocols defined according to internationally accepted standards and guidelines. The GPCR only registers tumors with malignant behaviors; in other words, the GPCR does not register benign tumors or those with uncertain behavior. All diagnostic and therapeutic centers including those in private and public sectors throughout the Golestan province are sources of data for the GPCR and the registry regularly receives information on cancer-related deaths from the health department of the Golestan University of Medical Science (GOUMS). In addition, the GPCR collects data from sources outside of the catchment area to limit underestimation due to patients’ referral to neighboring provinces including Tehran and Khorasan Razavi. The third version of the International Classification of Diseases for Oncology (ICD-O-3) system is used for coding tumors.

After obtaining the data, we used the CanReg 5 software for analysis. We calculated the age-specific rates, crude rates and age-standardized incidence rates (ASR), the latter using the world standard population, and presented per 100,000 person-years. Corresponding population data were obtained from the Statistics Office of the Deputy of Health of GOUMS. We used the Joinpoint regression analysis to quantify time trends over the study period using the average annual percent change (AAPC) and its corresponding 95% confidence intervals (95% CI). We used the Joinpoint Regression Program (version 4.6.0.0. April, 2018) for this analysis. The study was approved by the Ethics Committee of the GOUMS.

Results

In total, there were 898 new cases of lymphoma registered in the GPCR. The number (ASR) of NHL were 439 (6.5) and 231 (3.4) in males and females, respectively, with the median age of patients at 50 years. The corresponding numbers (ASR) of HL were 126 (1.5) and 102 (1.1) in males and females, respectively, with a median age of HL patients at 30 years. Table 1 shows the number of cases and ASR of lymphomas by type by 5-year period.

Table 1. Number and Age-Standardized Incidence Rate (Per 100,000 Person-Year) of Hodgkin Lymphoma and Non-Hodgkin Lymphoma in Golestan, Iran from 2004 to 2013

<table>
<thead>
<tr>
<th>Year</th>
<th>Males</th>
<th>ASR</th>
<th>Females</th>
<th>ASR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td></td>
<td>Number</td>
<td></td>
</tr>
<tr>
<td>2004</td>
<td>11</td>
<td>1.7</td>
<td>5</td>
<td>0.6</td>
</tr>
<tr>
<td>2005</td>
<td>14</td>
<td>1.6</td>
<td>8</td>
<td>0.8</td>
</tr>
<tr>
<td>2006</td>
<td>17</td>
<td>2.2</td>
<td>6</td>
<td>0.7</td>
</tr>
<tr>
<td>2007</td>
<td>16</td>
<td>1.6</td>
<td>15</td>
<td>1.7</td>
</tr>
<tr>
<td>2008</td>
<td>7</td>
<td>0.8</td>
<td>18</td>
<td>2.1</td>
</tr>
<tr>
<td>2009</td>
<td>16</td>
<td>2</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>2010</td>
<td>8</td>
<td>1</td>
<td>9</td>
<td>0.8</td>
</tr>
<tr>
<td>2011</td>
<td>12</td>
<td>1.1</td>
<td>8</td>
<td>0.9</td>
</tr>
<tr>
<td>2012</td>
<td>11</td>
<td>1.3</td>
<td>13</td>
<td>1.4</td>
</tr>
</tbody>
</table>

HL, Hodgkin lymphoma; NHL, non-Hodgkin lymphoma; ASR, age-standardized incidence rate.

Figure 3 shows the time trends of incidence of lymphoma in men (AAPC = -0.1; 95%CI: -6.05 to 60.9) and women (AAPC = 0.55; 95%CI: -4.36 to 5.72) over the last decade (Figure 2).

Our results also suggested no significant changes in incidence of NHL during the study period in men (AAPC = 0.8; 95CI%: -6.1 to 8.2) and women (AAPC = -0.1; 95CI%: -4.5 to 4.6), but there was a significant difference in time trends of HL between men and women (P value = 0.001), suggesting that the incidence of HL decreased in men (AAPC = -3.2; 95CI%: -10.9 to 5.1) and increased in women (AAPC = 3.6; 95CI%: -6.7 to 15).

Figure 3 shows the time trends of incidence of lymphoma in residents of urban and rural areas. The incidence rates of lymphoma were considerably higher in the urban population (ASR = 7.3) compared to the rural area (ASR = 2.9).
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Discussion

In this study, the incidence of lymphoma was reported in the Golestan province of northern Iran for the 10-year period 2004–2013. Other studies from Iran have reported much lower rates for HL than seen in our respective ASR of 1.5 and 1.1 in men and women, for example, in the Khouzestan (0.9 and 0.7 in males and females, respectively)\(^{15}\) and Fars (0.9 and 0.5 in males and females)\(^{16}\) provinces of Iran. In contrast, the ASR of NHL of 6.5 and 3.4 in men and women, respectively, are high relative to both Khuzestan (1.08 and 0.74 in males and females, respectively)\(^{15}\) and Fars (2.7 and 1.2 in males and females, respectively).\(^{16}\) Further, significantly higher rates of NHL were seen in men than women in Golestan (male to female ratio: 1.9); a finding which is in line with previous reports from India (M:F ratio 1.6), whereas studies in North America and Europe show the ratios to be close to unity.\(^{17}\) The underlying reasons for these observations are not clear, although one possible explanation might be occupational exposure; agriculture remains a major source of income and direct or indirect employment in Golestan, particularly among men, and exposure to agricultural pesticides and fertilizers are recognized as potentially important occupational hazards that confer an increased risk of NHL.\(^{18,19}\) In addition, exposure to certain infections including Helicobacter pylori infection has been suggested as a risk factor for NHL;\(^{20}\) a high prevalence of H. pylori infection in the adult and child population has been reported in Golestan province.\(^{21,22}\) Further studies are recommended to clarify the local risk factors for NHL in this population.

We did not find significant temporal variations in incidence rates of lymphoma in either men or women. However, there was a significant difference in the trends of HL between males and females. The observation that incidence rates of HL decreased in men but increased in women may reflect real trends in the prevalence of risk factors although changes in access to diagnostic services cannot be discounted. Further longitudinal studies

Figure 1. Age-Specific Incidence Rates (Per 100,000 Person-Year) of Lymphomas in Golestan, Iran during 2004–2013.

Figure 2. Temporal Variations in Age Standardized Incidence Rates (ASR) of lymphomas in Golestan, Iran, by Gender, During 2004–2013. AAPC, Average annual percent change; CI, confidence interval.

Figure 3. Time Trends in Age-Standardized Incidence Rates (ASR) of lymphomas in Urban and Rural Areas of Golestan Province, During 2004–2013. AAPC, Average annual percent change; CI, confidence interval.
with extended time periods are needed to assess the epidemiological transition of lymphomas in Golestan.

Our results suggested significantly higher rates for NHL in men than women (male to female ratio: 1.9). This finding is in line with previous reports from other Asian countries such as India (male to female ratio: 1.6), while studies from developed countries suggest almost similar rates for NHL in men and women in North America (1.2) and Europe (1.1). The differences in NHL rates between men and women in our population may partly be explained by higher exposure to risk factors including occupational exposure and agricultural pesticide in men compared to women.

The median age of our NHL and HL patients was 50 and 30 years, respectively. These findings were almost similar to other Asian countries, and was considerably lower than those reported for Western populations. The younger age of our lymphoma patients may be due to higher rates of risk factors including the Westernized lifestyle in our young population. The high proportions of young adult in Golestan population may also partly explain the higher rates of lymphoma in earlier age decades in this region. Further studies should be conducted to investigate the gender and age discrepancies in the incidence of lymphomas in our population.

Our results suggest higher incidence rates of lymphomas in urban population compared to rural areas, which may suggest that specific lifestyle or environmental factors may place the urban population at higher risk of lymphoma, such as air pollutants. We found higher incidence for lymphoma in western parts of the Golestan province including Gorgan city, the capital of the province. It is postulated that residents in Western Golestan may be more exposed to risk factors linked to urbanization relative to the population of Eastern Golestan. In addition, there are different major ethnic groups in the western (Fars ethnicity) compared with the eastern subdivision (Turkmen ethnicity) of Golestan, and this may also partly explain the differences.

The major advantage of this study is the high quality of cancer data from the GPCR. The GPCR is an ongoing population-based cancer registry and previous reports suggest that the quality of the GPCR data is high, its data has been approved by international authorities including the International Agency for Research on Cancer (IARC) and the IACR. The major limitation of this paper was lack of risk factor data. Because of this limitation, we could not explain the observed differences in incidence rate of lymphomas between different geographical regions. Therefore, it is recommended to conduct further studies focusing on risk factors of lymphomas in our population.

In conclusion, our study showed high incidence rates and a male predominance of NHL in the Golestan province. Further epidemiological studies should be conducted to better assess the underlying risk factors in our population to support future prevention strategies.

Authors’ Contribution
NJD collaborated in data processing, collaborated in analysis and wrote the manuscript. MNT conceptualized and designed the study, edited and critically reviewed manuscript. AF, MA and EH initiated, conceptualized and designed the study, edited and critically reviewed manuscript. SMS and MP interpreted results and critically reviewed manuscript. MG and AM collaborated in collection of data and critically reviewed manuscript. SHH, FGK, FB and FS edited, critically reviewed manuscript and collaborated in quality control. GR performed statistical analysis and wrote the manuscript. All authors read and approved the final manuscript.

Conflict of Interest Disclosures
Authors had no conflict of interest to declare.

Ethical Statement
Ethical issues of this study have been approved by ethics committee of Golestan University of Medical Sciences.

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References


