Arch Iran Med. March 2020;23(3):150-154

http www.aimjournal.ir

ARCHIVES OF IRANIAN MEDICINE

Open Access

Original Article

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

Nastaran Jafari-Delouei, MSc[1]; Mohammad Naimi-Tabiei, MD[2*]; Abdolreza Fazel, MD[3]; Mohammad Ashaari, MD[4]; Ehsan Hatami, MD[5]; Seyed Mehdi Sedaghat, MD[6]; Mohammad Poorabbasi, MD[7]; Susan Hasanpour-Heidari, MSc[1]; Fatemeh Ghasemi-Kebria, MSc[1]; Faezeh Salamat, MSc[1]; Abbas Moghaddami, MD[3]; Masoomeh Gholami, MSc[7]; Freddie Bray, PhD[8]; Gholamreza Roshandel, MD, PhD[1]

[1]Golestan Research Center of Gastroenterology and Hepatology, Golestan University of Medical Sciences, Gorgan, Iran
[2]Cancer Research Center, Golestan University of Medical Sciences, Gorgan, Iran
[3]Omid Cancer Research Center, Omid Preventive Medicine and Heath Promotion Center, Golestan University of Medical Sciences, Gorgan, Iran
[4]Department of Pathology, Sayyad Shirazi Hospital, Golestan University of Medical Sciences, Gorgan, Iran
[5]Mirdamad Radiotherapy and Chemotherapy Center, Gorgan, Iran
[6]Deputy of Public Health, Golestan University of Medical Sciences, Gorgan, Iran
[7]Death Registry Unit, Deputy of Public Health, Golestan University of Medical Sciences, Gorgan, Iran
[8]Section of Cancer Surveillance, International Agency for Research on Cancer, Lyon, France

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, joinpoint 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

Cite this article as: Jafari-Delouei N, Naimi-Tabiei M, Fazel A, Ashaari M, Hatami E, Sedaghat SM, et al. Descriptive epidemiology of lymphoma in Northern Iran: results from the Golestan Registry 2004–2013. Arch Iran Med. 2020;23(3):150–154.

Received: April 16, 2019, Accepted: December 7, 2019, ePublished: March 1, 2020

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,[3] 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

***Corresponding Author:** Mohammad Naimi-Tabiei, MD; Cancer Research Center, Sayyad Shirazi Hospital, Sayyad Shirazi Bulevard, Gorgan, Iran. Tel: +98 32251910; Email: grcgh.grcgh@gmail.com

a high-risk region for upper gastrointestinal cancers during the last 50 years.[7,8] The Golestan Population-based Cancer Registry (GPCR), as a voting member of the International Association of Cancer Registries (IACR), has provided high-quality cancer statistics for the Golestan population since 2004.[9,10] In this paper, we aimed to present the incidence rates and describe the geographic and temporal variations in lymphomas in the Golestan province over the 10-year period from 2004 to 2013.

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.[10] 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.[11]

After obtaining the data, we used the CanReg 5 software for analysis.[12] We calculated the age-specific rates, crude rates and age standardized incidence rates (ASR), the latter using the world standard population,[13] 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[14] 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. Figure 1 shows the age-specific rates of HL and NHL in men and women. It suggests that the NHL peaks at the age group 75–79 and 70–74 in men and women, respectively.

According to the results of the joinpoint analysis, there was no significant temporal trends in incidence of lymphoma in men (AAPC = -0.16; 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

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

Year	HL				NHL			
	Males		Females		Males		Females	
	Number	ASR	Number	ASR	Number	ASR	Number	ASR
2004	11	1.7	5	0.6	23	3.7	22	3.6
2005	14	1.6	8	0.8	48	8	22	3.5
2006	17	2.2	6	0.7	45	7.6	18	2.9
2007	16	1.6	15	1.7	41	6.2	25	3.6
2008	7	0.8	18	2.1	49	6.4	24	3.8
2009	16	2	10	1	50	8	15	2.2
2010	8	1	9	0.8	49	7.5	24	3.2
2011	12	1.1	8	0.9	33	4.2	29	3.6
2012	11	1.3	13	1.4	52	6.4	27	3.9
2013	14	1.7	10	0.9	49	6.5	25	3.2

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

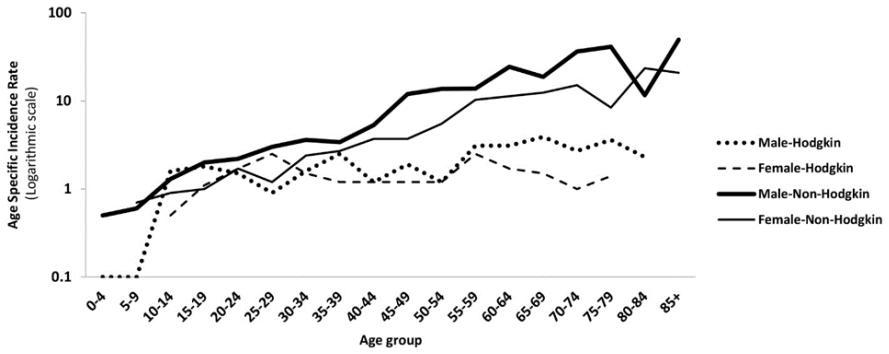

Figure 1. Age-Specific Incidence Rates (Per 100 000 Person-Year) of Lymphomas in Golestan, Iran during 2004–2013.

= 5.3) (*P* value = 0.054). The geographical distribution of lymphomas in subdivisions of the Golestan province are shown in Figure 4; incidence rates for both HL and NHL are highest in the western parts of the province.

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 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

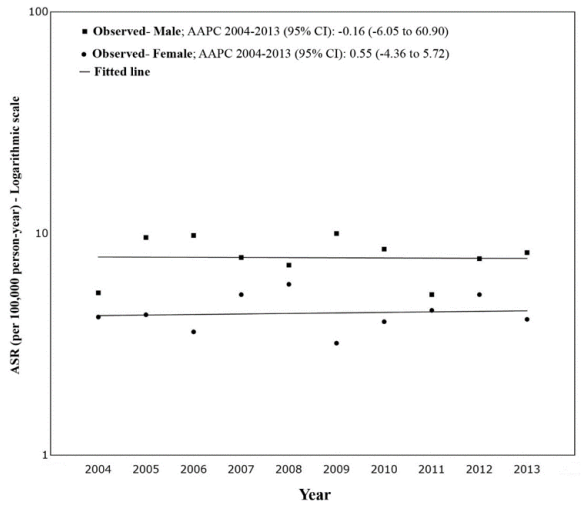

Figure 2. Temporal Variations in Age Standardized Incidence Rates (ASR) of Lymphomas in Golestan, Iran, by Gender, During 2004-2013. AAPC, Average annual percent change; CI, confidence interval.

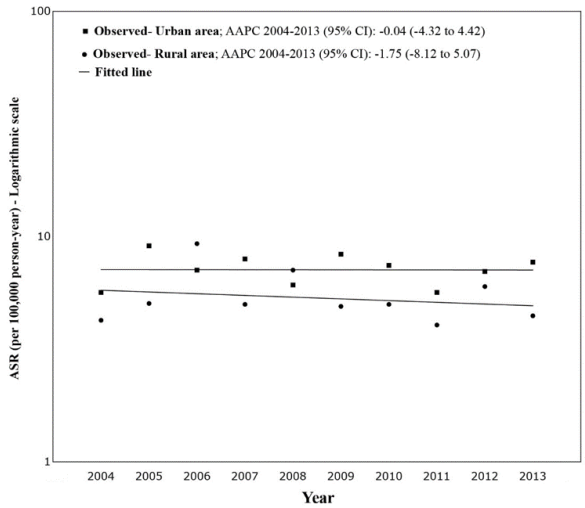

Figure 3. Time Trends in Age-Standardized Incidence Rates (ASR) of Lymphomas in Urban and Rural Areas of Golestan Province, During 2004–2013. AAPC, Average annual percent change; CI, confidence interval.

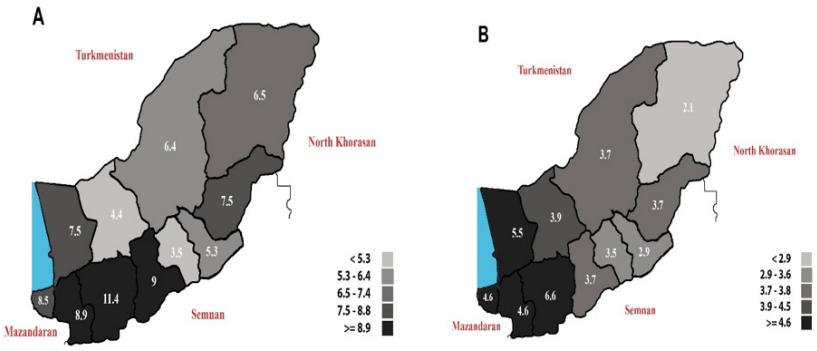

Figure 4. Geographical Distribution of Age-Standardized Incidence Rates (ASR) (Per 100 000 Person-Year) of Lymphomas in Golestan, Iran, 2004-2013. (A) Male, (B) Female.

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).[17] 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,[23,24] and was considerably lower than those reported for Western populations.[17] 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[25,26] of lymphoma, such as air pollutants.[27,28] 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.[29]

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[9,10]; its data has been approved by international authorities including the International Agency for Research on Cancer (IARC) and the IACR.[2] 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 commiittee of Golestan University of Medical Sciences.

Acknowledgments

We greatly appreciate the efforts of the GPCR staff as well as all physicians and personnel of the GPCR sources throughout the Golestan province for their cooperation in the process of data collection. This project was funded by the Golestan University of Medical Sciences under contract 35-306385.

References

1. Bray F, Ferlay J, Soerjomataram I, Siegel R L, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates

of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394-424. doi:10.3322/caac.21492.
2. WHO, International Agency for Research on Cancer. Cancer incidence in five continents. Available from: http://ci5.iarc.fr. Accessed January 2019.
3. Etemad-Moghadam S, Tirgary F, Keshavarz S, Alaeddini M. Head and neck non-Hodgkin's lymphoma: a 20-year demographic study of 381 cases. Int J Oral Maxillofac Surg. 2010;39(9):869-72. doi:10.1016/j.ijom.2010.03.029.
4. Baharvand M, Mortazavi H. Characteristics of Hodgkin lymphoma in a defined group of Iranian pediatric patients. Asian Pac J Cancer Prev. 2014;15(13):5167-9. doi:10.7314/APJCP.2014.15.13.5167.
5. Saxena N, Hartman M, Bhoo-Pathy N, Lim JN, Aw TC, Iau P, et al. Breast cancer in South East Asia: comparison of presentation and outcome between a middle income and a high income country. World J Surg. 2012;36(12):2838-46. doi:10.1007/s00268-012-1746-2.
6. International Agency for Research on Cancer. WHO. CANCER TODAY: Data visualization tools for exploring the global cancer burden in 2018. Accessed March 17, 2019. Available from: https://gco.iarc.fr/today.
7. Mahboubi E, Kmet J, Cook PJ, Day NE, Ghadirian P, Salmasizadeh S. Oesophageal cancer studies in the Caspian Littoral of Iran: the Caspian cancer registry. Br J Cancer. 1973;28(3):197-214. doi:10.1038/bjc.1973.138.
8. Kmet J, Mahboubi E. Esophageal cancer in the Caspian littoral of Iran: initial studies. Science. 1972;175(4024):846-53. doi:10.1126/science.175.4024.846
9. Roshandel G, Sadjadi A, Aarabi M, Keshtkar A, Sedaghat SM, Nouraie SM, et al. Cancer incidence in Golestan Province: report of an ongoing population-based cancer registry in Iran between 2004 and 2008. Arch Iran Med. 2012;15(4):196-200.
10. Roshandel G, Semnani S, Fazel A, Honarvar M, Taziki M, Sedaghat S, et al. Building cancer registries in a lower resource setting: The 10-year experience of Golestan, Northern Iran. Cancer Epidemiol. 2018;52:128-133. doi:10.1016/j.canep.2017.12.014.
11. Fritz A, Percy C, Jack A, Shanmugaratnam K, Sobin L, Parkin DM, et al. International classification of diseases for oncology (ICD-O-3). 3rd ed. Nonserial Publication; 2000.
12. Ervik M J, Cooke A P, Ferlay J, Rahimi A, Antomi S, Dhivar D, et al. CanReg5: Computer Software for Cancer Registries. Lyon: International Agency for Research on Cancer; 2008.
13. Segi M. Cancer mortality for selected sites in 24 countries (1950-1957). Sendai: Department of Public Health, Tohoku University of Medicine; 1960.
14. Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. Stat Med. 2000;19(3):335-51. doi:10.1002/(SICI)1097-0258(20000215)19:3<335::AID-SIM336>3.0.CO;2-Z.
15. Talaiezadeh A, Tabesh H, Sattari A, Ebrahimi S. Cancer incidence in southwest of iran: first report from Khuzestan population-based cancer registry, 2002-2009. Asian Pac J Cancer Prev. 2013;14(12):7517-22. doi:10.7314/APJCP.2013.14.12.7517.
16. Masoompour SM, Yarmohammadi H, Rezaianzadeh A, Lankarani KB. Cancer incidence in southern Iran, 1998–2002: Results of population-based cancer registry. Cancer Epidemiol. 2011;35(5):e42-e47. doi:10.1016/j.canep.2011.05.018.
17. Nair R, Arora N, Mallath MK. Epidemiology of Non-Hodgkin's Lymphoma in India. Oncology. 2016;91 suppl 1:18-25. doi:10.1159/000447577.
18. Hu L, Luo D, Zhou T, Tao Y, Feng J, Mei S. The association between non-Hodgkin lymphoma and organophosphate pesticides exposure: A meta-analysis. Environ Pollut. 2017;231(Pt 1):319-28. doi:10.1016/j.envpol.2017.08.028.
19. Luo D, Zhou T, Tao Y, Feng Y, Shen X, Mei S. Exposure to organochlorine pesticides and non-Hodgkin lymphoma: a meta-analysis of observational studies. Sci Rep. 2016;6:25768. doi:10.1038/srep25768.
20. Floch P, Megraud F, Lehours P. Helicobacter pylori Strains and Gastric MALT Lymphoma. Toxins. 2017;9(4):132. doi:10.3390/toxins9040132.
21. Ghasemi-Kebria F, Ghaemi E, Azadfar S, Roshandel G. Epidemiology of Helicobacter pylori infection among Iranian children. Arab J Gastroenterol. 2013;14(4):169-72. doi.org/:10.1016/j.ajg.2013.11.002.
22. Ghasemi Kebria F, Bagheri H, Semnani S, Ghaemi E. Seroprevalence of anti-Hp and anti-cagA antibodies among healthy persons in Golestan province, northeast of Iran (2010). Caspian J Intern Med. 2011;2(3):256-60.
23. Prakash G, Sharma A, Raina V, Kumar L, Sharma MC, Mohanti BK. B cell non-Hodgkin's lymphoma: experience from a tertiary care cancer center. Ann Hematol. 2012;91(10):1603-11. doi:10.1007/s00277-012-1491-5.
24. Mozaheb Z, Aledavood A, Farzad F. Distributions of major subtypes of lymphoid malignancies among adults in Mashhad, Iran. Cancer Epidemiol. 2011;35(1):26-9. doi:10.1016/j.canep.2010.09.009.
25. Salati M, Cesaretti M, Macchia M, Mistiri ME, Federico M. Epidemiological overview of Hodgkin lymphoma across the Mediterranean Basin. Mediterr J Hematol Infect Dis. 2014;6(1):e2014048.
26. Morton LM, Slager SL, Cerhan JR, Wang SS, Vajdic CM, Skibola CF, et al. Etiologic heterogeneity among non-Hodgkin lymphoma subtypes: the InterLymph Non-Hodgkin Lymphoma Subtypes Project. J Natl Cancer Inst Monogr. 2014;2014(48):130-44. doi:10.1093/jncimonographs/lgu013.
27. Richardson D B, Terschüren C, Hoffmann W. Occupational risk factors for non-Hodgkin's lymphoma: A population-based case–control study in Northern Germany. Am J Ind Med. 2008;51(4):258-268. doi:10.1002/ajim.20552.
28. Ramis R, Vidal E, García-Pérez J, Lope V, Aragonés N, Pérez-Gómez B, et al. Study of non-Hodgkin's lymphoma mortality associated with industrial pollution in Spain, using Poisson models. BMC Public Health. 2009;9(1):26. doi:10.1186/1471-2458-9-26.
29. Kleinstern G, Abu Seir R, Perlman R, Khatib A, Abdeen Z, Elyan H, et al. Ethnic variation in medical and lifestyle risk factors for B cell non-Hodgkin lymphoma: A case-control study among Israelis and Palestinians. PLoS One. 2017;12(2):e0171709. doi:10.1371/journal.pone.0171709.