American Journal of Cancer Prevention, 2015, Vol. 3, No. 5, 96-99
Available online at http://pubs.sciepub.com/ajcp/3/5/6

DOI:10.12691/ajcp-3-5-6

The Survival of Extra nodal Non-Hodgkin's Lymphoma Patients in the West of Iran

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Received May 20, 2015; Revised September 10, 2015; Accepted October 07, 2015

Abstract **Background**: Extra nodal Non-Hodgkin's Lymphoma (NHL) is a heterogeneous disease in regard to geographical, ethnic, anatomic, etiological, and morphological diversities. The aim of study is evaluation of survival in extra nodal NHL patients for the first time in western Iran. **Patients and Methods**: Between of 2002 to 2014, fifty patients with extra nodal NHL referred to Our Clinic. We checked age, sex, histopathology reports, anatomic sites and survival for them. One representative Material of patients with diffuse large B-cell lymphoma (DLBL), Malt lymphoma, FL, SLL, anaplastic lymphoma and Burkitt's lymphomas was re-classified after revision. The overall survival (OS) was plotted by GraphPad Prism 5 software. **Results**: The median age at diagnosis for the patients was 50 years (range, 13-77 years) that 26 patients (52%) had age≤ 50 years. Twenty-seven patients (54%) were male. Involvement anatomic sites were GIT, bone, abdominal, testis, skin, CNS, spleen, maxilla and adrenal gland for 19 patients(38%), 15(30%), 5(10%), 4(8%), 2(4%), 2(4%), 1(2%), 1(2%) and 1(2%), respectively. The 3-year, 5-year and 10-year survival rates are 70%, 62.2% and 60.8%, respectively. **Conclusion**: The OS in this study is higher than other studies and the median age is lower. Also, GIT is the most common site of involvement in extra nodal lymphomas in Middle East.

Keywords: *NHL, overall survival, extra nodal lymphoma, DLBCL*

Cite This Article: Mehrdad Payandeh, Masoud Sadeghi, Edris Sadeghi, and Mehrnoush Aeinfar, "The Survival of Extra nodal Non-Hodgkin's Lymphoma Patients in the West of Iran." *American Journal of Cancer Prevention*, vol. 3, no. 5 (2015): 96-99. doi: 10.12691/ajcp-3-5-6.

1. Introduction

NHL (Non-Hodgkin's Lymphoma) arise either in lymph nodes and in other lymphatic tissues, such as the tonsils, spleen, Waldeyer's ring and thymus ("nodal" lymphomas), or in lymphatic cells in other organs ("extra-nodal" lymphomas) [1].

Extra nodal NHLs have been reported to originate from almost every anatomic site of the body such as gastrointestinal tract (most common), head and neck (Waldeyer's ring, nose/paranasal sinses/nasopharynx, salivary glands, etc.), skin, central nervous system (CNS), bone, testis, thyroid, breast, orbit, and rarely adrenal, pancreas, and the genitourinary tract [2].

Differences in presentation, behavior and survival between non-Hodgkin's lymphomas at different primary sites have led several authors to suggest that nodal and extra-nodal disease should be considered as distinct entities with differing aetiologies [3]. Furthermore, there is compelling evidence that specific local factors may play an aetiological role in the development of lymphomas at certain extra-nodal sites *e.g., Helicobacter pylori* infection is associated with primary gastric lymphoma, but not with lymphomas at other sites [4].

The aim of study is evaluation of survival in extra nodal NHL patients for the first time in western Iran.

2. Patients and Methods

Between of 2002 to 2014, fifty patients with extra nodal NHL referred to Our Clinic, Kermanshah City, Iran. We checked age, sex, histopathology reports, anatomic sites and survival for them.

Once a diagnosis of NHL was made by the hospital pathologist, slides and frozen material were sent for review to a panel of four regional pathologists, experienced in hemato-pathology. Immunohistochemical (IHC) stains using antibodies against CD 20, CD 3, CD 10, CD 5, CD 23, BCL2 and cyclinD1 were done in each case. The cases were diagnosed by morphology on H and E sections and IHC profile according to WHO classification of lymphoid neoplasms by senior histopathologists. At last, extra nodal patients entered to our study.

One representative Material of patients with diffuse large B-cell lymphoma (DLBCL), Malt lymphoma, follicular lymphoma (FL), small lymphocytic lymphoma (SLL), anaplastic lymphoma and Burkitt's lymphomas was re-classified after revision. The overall survival (OS) was plotted by GraphPad Prism 5 software.

3. Results

Table 1. the characteristics for Extra nodal Non-Hodgkin's Lymphoma (n=50)

Characteristics	n(%)	Median ±SD	Range
Age(year)			
Age group(year)			
≤50	26(52)		
>50	24(48)		
Sex			
Male	27(54)		
Female	23(46)		
Histopathology			
DLBCL	34(68)		
Malt Lymphoma	5(10)		
Burkitt Lymphoma	4(8)		
FL	4(8)		
SLL	1(2)	50±17.06	13-77
T-cell Lymphoma	1(2)		
Anaplastic Lymphoma	1(2)		
Anatomic sites			
GIT	19(38)		
Bone	15(30)		
Abdominal	5(10)		
Testis	4(8)		
Skin	2(4)		
CNS	2(4)		
Spleen	1(2)		
Maxilla	1(2)		
Adrenal gland	1(2)		

DLBCL: diffuse large B cell lymphoma, FL: follicular lymphoma, SLL: small lymphocytic lymphoma, GIT: gastrointestinal tract, CNS: central nervous system

The median age at diagnosis for the patients was 50±17.06 years (range, 13-77 years) that 26 patients (52%) had age≤ 50 years and 24(48%) had age>50 years (Table 1). Twenty-seven patients (54%) were male and 23(46%) were female. Histopathology reports showed that 34 patients (68%), 5(10%), 4(8%), 4(8%), 1(2%), 1(2%) and 1(2%) had DLBCL (Figure 1), Malt, Burkitt, FL, SLL, T-cell and anaplastic lymphoma, respectively. Involvement anatomic sites were small lymphocytic lymphoma (GIT), bone, abdominal, testis, skin, central nervous system (CNS), spleen, maxilla and adrenal gland for 19 patients (38%), 15(30%), 5(10%), 4(8%), 2(4%), 2(4%), 1(2%), 1(2%) and 1(2%), respectively.

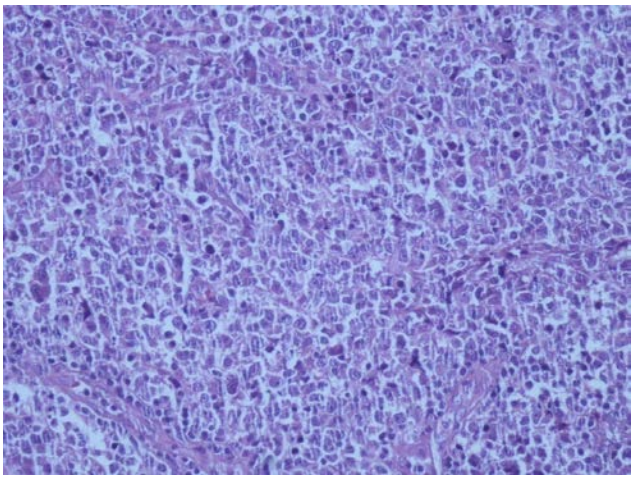

Figure 1. Histopathology image for Diffuse large B-cell lymphoma(×200)

The Figure 2 shows 3-year, 5-year and 10-year OS for all patients. The 3-year, 5-year and 10-year mean survivals are 25, 32 and 78.5 months, respectively. Also, the 3-year, 5-year and 10-year survival rates are 70%, 62.2% and 60.8%, respectively.

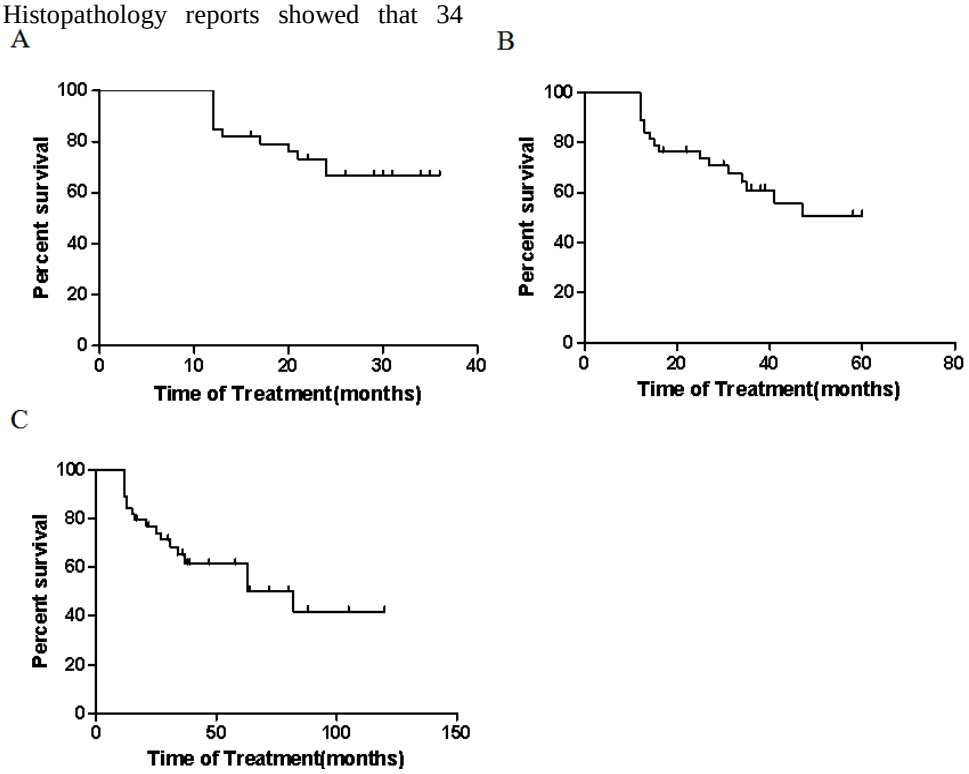

Figure 2. The overall survival for all patients (A) 3-year (B) 5-year (C) 10-year

The 3-year, 5-year and 10-year OS for all patients based on sex has been written in Figure 3. There was no significant correlation between male and female for 3-year, 5-year and 10-year periods (P>0.05). The 3-year, 5-year and 10-year mean survival was 24.5, 32.7 and 41 months for males and also 25.2, 30.7 and 39.2 months for females, respectively. The 3-year, 5-year and 10-year survival rates were 68.2%, 65.2% and 65.2% for males and also 72.2%, 59.1% and 59.1% for females, respectively.

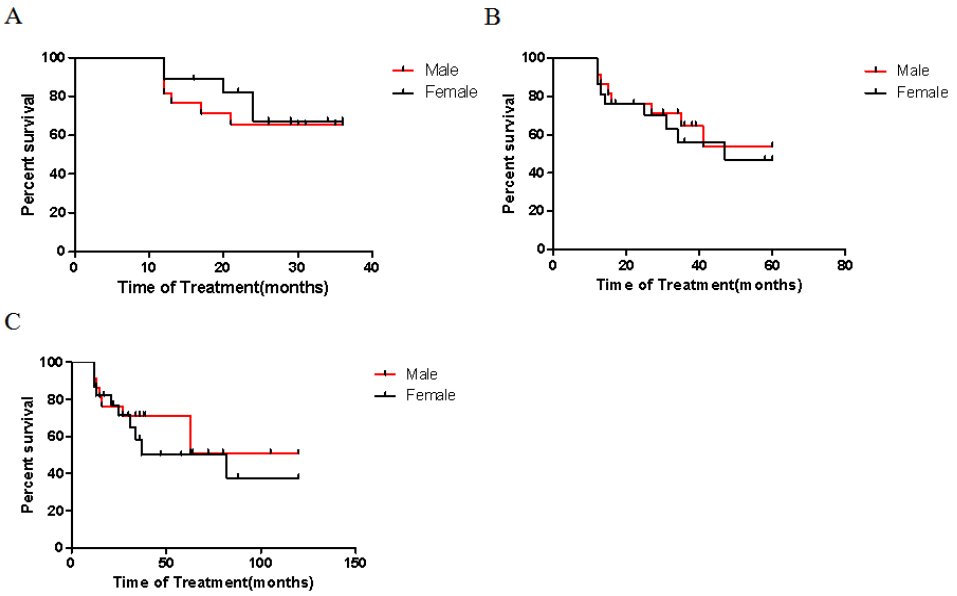

Figure 3. The overall survival for all patients based on sex (A) 3-year (B) 5-year (C) 10-year

The 3-year, 5-year and 10-year OS for all patients based on age group has been written in Figure 4. There was no significant correlation between patients with age≤ 50 years and age>50 years for 3-year, 5-year and 10-year periods (P>0.05). The 3-year, 5-year and 10-year mean survival was 27.1, 36.1 and 47.1 months for age group≤ 50 years and also 21.7, 26.3 and 31.8 months for age group>50 years, respectively. The 3-year, 5-year and 10-year survival rates were 69.7%, 64% and 64% for age group≤ 50 years and also 70.6%, 60% and 57.1% for age group>50 years, respectively.

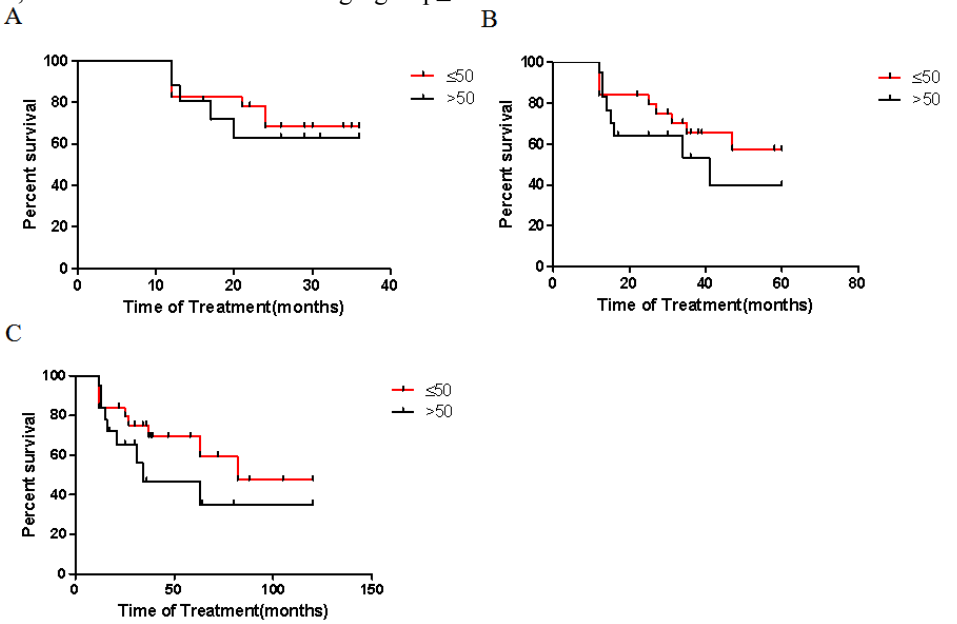

Figure 4. The overall survival for all patients based on age group (A) 3-year (B) 5-year (C) 10-year

4. Discussion

Extra nodal NHL is a heterogeneous disease in regard to geographical, ethnic, anatomic, etiological, and morphological diversities [5]. Studies from Western countries have reported the occurrence of extra nodal NHL as 24-48% of all NHLs [6].

GIT is reported to be the most common site of involvement in extra nodal lymphomas and its incidence is rising throughout the world [7]. Relatively high incidence rates of small-intestinal lymphoma have been reported before in the Middle East [8] and are a result of the presence of a distinct disease entity, immunoproliferative small-intestinal disease, or so-called Mediterranean lymphoma. This may partly explain the relative excess of small-intestinal lymphoma in Kuwait. Similarly, high rates of gastric lymphoma have been noted in parts of Northern Italy [9]. In our study, GIT was the most percent (38%) for extra nodal NHL similar to Krol et al. [10] results.

Extra nodal disease is the predominant disease manifestation (incidence, about 40%) among DLBCL patients. Even in patients with stage I disease, 56% had extra nodal DLBCL [10]. Compared to the western and Middle East countries, low incidence of DLBCL among Asians and high incidence of NK/T cell lymphomas at head neck region possibly explains these diversities [11].

In spite of alarming increase in incidence of Primary central nervous system lymphoma (PCNL) in the West (because of HIV/AIDS), the incidence is fairly low or at least, stable in the Middle East and Asian countries, including India [12]. In our study (Middle East, Iran), DLBCL was the most percent (68%) and CNS involvement similar to other Asian countries was low (2%) compared to the West. NHL is a malignancy that occurs frequently in the elderly with a median age greater than 60 years. However, most chemotherapy trials have included predominantly patients less than 60 years of age [13].

NHL Patients in a study ranged in age from 15 to 91 years (median, 63) that overall 5-year survival was 42%. (13) An analysis of prognostic factors has been performed on 260 patients with high and intermediate grade NHL that the overall 5-year survival rate was 50% [14]. Other study showed that median age for extra nodal NHL was 67 years (range, 7-94) [10]. In our study, the median survival was 50 years for extra nodal NHL that this median age is lower than other studies and also the 5-year survival rate was 62.2% that survival rate in this study is higher than other studies. The 10-year survival in this study is higher than the 5-year survival in other studies. Therefore, mortality after 5 years in extra nodal NHL patients is less compared to the first 5-year. In this study, there is no significant correlation between sex and age group with the OS.

5. Conclusion

The OS in this study is higher than other studies and the median age is lower. Also, GIT is the most common site of involvement in extra nodal lymphomas in Middle East.

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