

The Association between Comorbidity and Survivorship among non-Hodgkin lymphoma Patients in Albania

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Abstract: Background: Non-Hodgkin Lymphomas (NHL) are malignancies that affect patient survival. The aim of this study is to assess the association between comorbidity and NHL survivorship in a group of NHL patients in Albania. Methods: A total of 107 patients newly diagnosed with NHLs and followed-up during 2011-2015 in the premises of Hematology Service of University Hospital Center "Mother Teresa" in Tirana, the capital of Albania, were included in the survey. All patients with existing NHLs were excluded. Kaplan-Meier test was used to assess patients survival during 2011-2015 and Cox Regression test was used to determine the risk of dying from NHLs during this period. Results: Mean age of participants was 57.7 years and 61.7% were males. About half of patients (44.9%) had at least one concomitant disease at the time of diagnosis. The overall 50 months survival was 57.2%, being significantly lower among NHL patients with comorbidity. Comorbidity NHL patients had a significantly twofold higher risk of dying from NHLs compared to NHL patients without concomitant diseases at the time of diagnosis. Conclusion: Presence of comorbidity at the time of NHL diagnosis is associated with significantly shorter survival and significantly higher risk of death from NHLs.

Keywords: Albania, comorbidity, non-Hodgkin Lymphoma, prognosis, survival

1. Introduction

Non-Hodgkin Lymphoma (NHL), a complex group of malignant diseases originating from B and T lymphocytes, usually affect lymphoid tissues but they can literally affect any tissue of the body.^[1] NHL severity ranges from slowly progressing indolent lymphomas, such as follicular lymphoma (FL) to extremely aggressive ones such as diffuse large B cell lymphoma (DLBCL) and Burkitt lymphoma.^[1]

The etiologic factors of NHLs are generally not well understood but the international literature suggests that the main factors increasing the risk of NHLs include higher age and male sex,^[2] congenital or acquired immunosuppressive states,^[3,4] certain viruses including Epstein-Barr virus, hepatitis C virus, Kaposi's sarcoma herpes virus, etc.^[5,6] Also, other risk factors might include ultraviolet radiation, hair dyes among females, occupational exposures, genetic factors, etc.

The heterogeneity of NHLs^[7] is reflected in very different survival opportunities for the affected patients with more aggressive lymphomas showing worst overall survival. In general, the etiologic factors of NHLs also serve as predictors of worse NHL survival but there are other factors that could influence NHL survivorship, including unfavorable International Prognostic Index, performance status at the time of diagnosis, tumor stage, bone marrow involvement, etc.^[8,9] Despite the current knowledge about risk factors of NHL survival, the association between NHLs survivorship with the presence of other concomitant diseases has not been intensively studied. Especially in Albania, the information about NHL patients and factors associated with NHL survivorship is rather scarce. A recent survey has shed

light on these issues in Albania^[10] but the association between NHL survival and comorbidity has not yet been reported. In this context, the aim of this study is to assess the association between NHL survivorship and presence of comorbidity among a group of NHL patients in Albania.

2. Materials & Methods

The present study includes 107 patients newly diagnosed with NHLs at the premises of the Hematology Service of University Hospital Center "Mother Teresa", in Tirana, the capital of Albania, during 2011-2015. We excluded all patients previously known to suffer from NHLs and included only patients with a recent diagnosis of NHL.

At the moment of diagnosis, a range of data was collected for every patient meeting the inclusion criteria, including basic demographic information on age and gender, and other information was retrieved from various assessments and/or examinations, including the assessment of performance status of the patient, stage and grade of NHL, histologic type of NHLs, the mass of the biggest tumor, presence of B symptoms, lymphatic tissue or extranodal involvement, the International Prognostic Index and lactate dehydrogenase level. Also, we collected information on other diseases that study participants were suffering from at the time of NHL diagnosis. Most patients with concomitant diseases were suffering from diabetes, high blood pressure and liver cirrhosis. Such patients were classified as patients with comorbidity versus the remaining patients suffering only from the recently detected NHL.

At the end of the study period (in 2015) we meticulously retrieved and recorded the information about the life status

(dead or alive) of each participant. This variable is essential for calculating the survival of NHL patients included in the study.

The study was approved by the Board of Medical Bio-Ethics in the premises of the Faculty of Medicine.

We used the Kaplan-Meier test to calculate overall survival of NHL patients at the end of study period. Cox Regression test was used to assess the risk of dying from NHL, according to selected independent variables, reported in terms of hazard ratios (HR), through crude (unadjusted) and adjusted models.

The Statistical Package for Social Sciences software (SPSS), version 17 was used for all the statistical analysis.

3. Results

In total there were 107 patients included in the study. Their baseline characteristics (at the moment of diagnosis) are presented in Table 1.

The majority of study participants were males (61.7%) and the average age of patients was 57.7 years $\pm$ 12.7 years (range 16-78). Less than half of participants (44.9%) reported the presence of at least another disease apart from the newly diagnosed NHL; 33.6% of study participants reported at least another disease besides NHL, 10.3% reported two other diseases and 0.9% or one patient reported

three concomitant diseases at the time of NHL diagnosis (Table 1).

Table 1: Baseline characteristics of study subjects at the moment of NHL diagnosis

Study variable	Absolute number	Percentage
Total	107	100.0
Gender		
Male	66	61.7
Female	41	38.3
Age (years) - mean $\pm$ SD	57.7 $\pm$ 12.7	
Age-group		
16-54 years	35	32.7
55-63 years	35	32.7
64-78 years	37	34.6
Comorbidity		
No	59	55.1
Yes	48	44.9
Number of concomitant diseases		
None	59	55.1
One disease	36	33.6
Two diseases	11	10.3
Three diseases	1	0.9

Figure 1 shows the survival of NHL patients. By the end of study period (about 50 months after the diagnosis) the overall survival rate was 57.2%. Figure 2 shows that the survival of NHL patients is poorer among those with comorbidity and the difference is statistically significant.

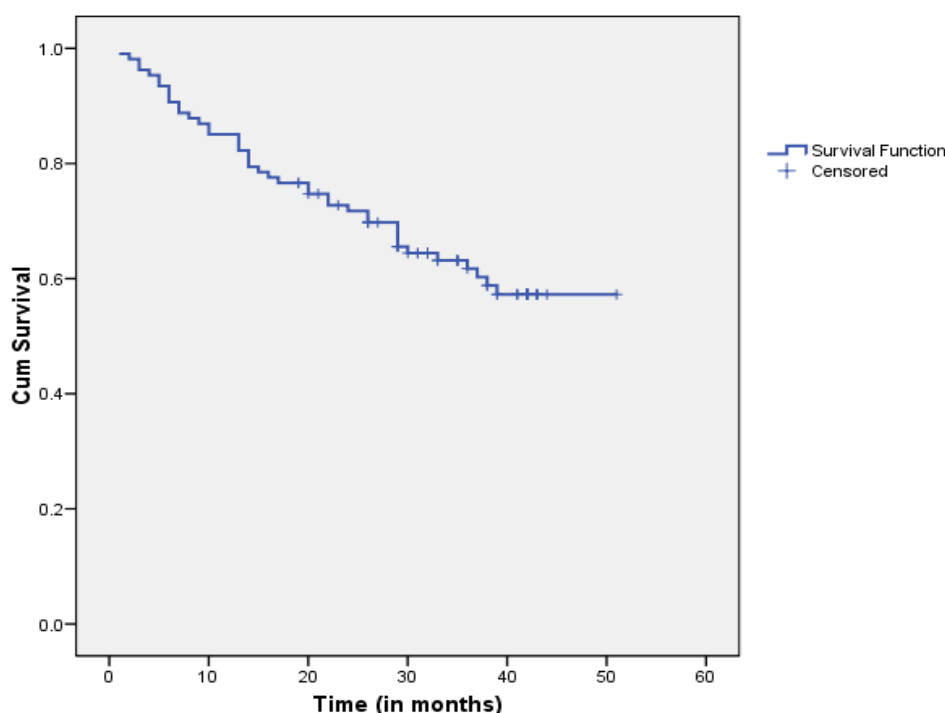


Figure 1: NHL overall survival

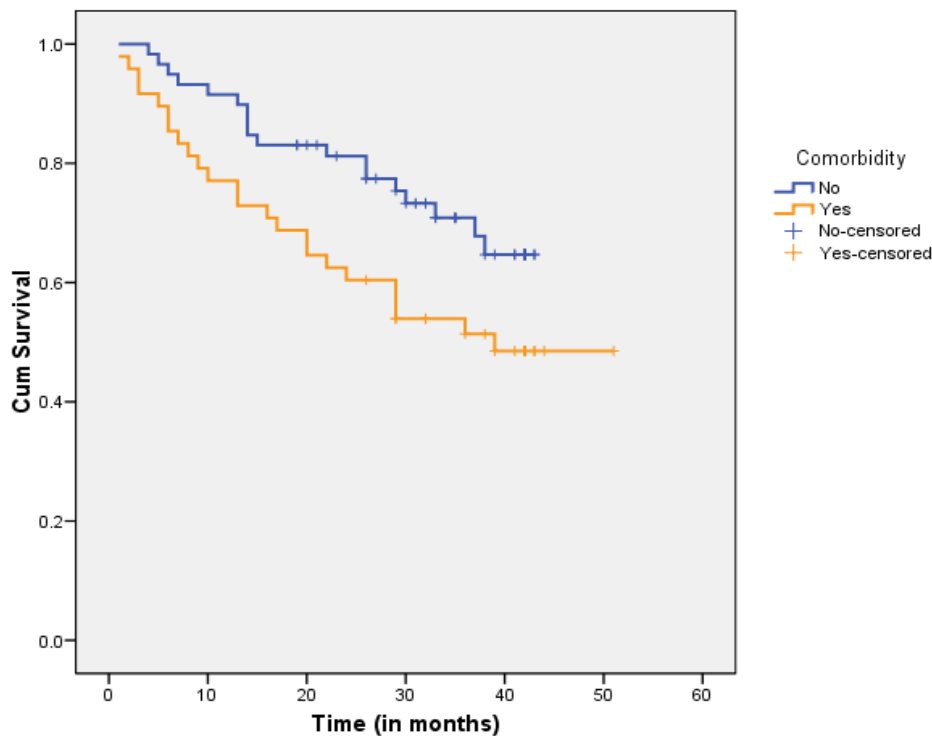


Figure 2: NHL survival by comorbidity status at the moment of diagnosis

Table 2 presents information about the risk of death from NHL according to comorbidity status and number of concomitant diseases assessed at the time of diagnosis (initiation of treatment). Presence of comorbidity significantly increases the risk of death from NHLs in crude (HR=1.8; P=0.049) and age-and-sex adjusted model (HR=2.0; P=0.041).

Table 2: Risk of death from NHL according to selected independent variables; hazard ratios (OR) from Cox Regression

Variable	Model 1 [†]		Model 2 [‡]	
	HR (95% CI)*	P-value	HR (95% CI)	P-value
Comorbidity status				
No	1.0 (reference)	-	1.0 (reference)	-
Yes	1.8 (1.0-3.4)	0.053	2.0 (1.0-3.8)	0.041

*HR: Risk of dying vs. being alive.

[†] Crude (unadjusted) models.

[‡] This model was simultaneously adjusted for age and sex

4. Discussion

The present study we reported scientific information about the association of non-Hodgkin survivorship and comorbidity among a group of 107 patients newly diagnosed with NHL in Albania, a small post-communist country in South-East Europe. To the best of our knowledge this is the first study addressing this research topic. Our findings suggest that about half (44.9%) of NHL patients in Albania suffer from at least another disease at the time their NHL is diagnosed. Also, the survival of NHL patients with concomitant diseases is significantly less favorable compared to NHL patients without comorbidities in crude and age-and-sex adjusted analysis.

Our findings regarding the association of comorbidity and NHL survivorship are supported by previous research in international arena. For example, the literature reports that patients suffering from NHLs and other concomitant diseases have a lower survival and a higher risk of death from treatment compared to NHL patients without comorbidities.^[11] A literature review investigating the association between diabetes and risk of non-Hodgkin lymphoma, reported that in prospective studies diabetes significantly increased the risk of NHLs by 1.2 folds.^[12] Additionally, other studies suggest that diabetes is an independent risk factor for NHLs.^[13] The association between NHLs and hepatic cirrhosis has also been documented in the literature.^[14,15] Another study among 904 NHL patients diagnosed between 1933-1996 in the Netherlands reported that the prevalence of comorbidity was 20% among patients less than 60 years old, but 43% among those aged 60-69 years old and 61% among patients 70 years old or older.^[16] The most common concomitant diseases were heart diseases, hypertension and diabetes mellitus,^[16] results that are very similar to our findings.

Yet another study reported that 45% of NHL patients aged more than 60 years had one or more concomitant diseases at the time of NHL diagnosis.^[17] In our study we reported that 44.9% of NHL patients in Albania had one or more concomitant diseases at the moment of diagnosis, thus being quite similar to international reports.

The association between unfavorable NHL survivorship with the presence of comorbidity at the moment of NHL diagnosis is reported by other international studies as well. A study among 381 patients diagnosed with NHL among 1995-1999 in the Netherlands reported that the risk of dying from NHLs was twofold higher among NHL patients with comorbidity at the moment of diagnosis compared to NHL patients without concomitant diseases.^[17] This result is

totally comparable to our findings, suggesting a hazard ratio (HR) of 2 ($P=0.041$) for the risk of dying from NHLs among patients with comorbidity compared to patients with no other diseases at the time of diagnosis, at age-and-sex adjusted analysis.

5. Conclusion

The presence of other diseases at the time of diagnosis of non-Hodgkin lymphoma is significantly associated with an unfavorable NHL survivorship among the respective patients. The finding highlights the importance of prevention and/or appropriate treatment and management of such diseases that, when overlooked, could be independent risk factors of death from non-Hodgkin lymphoma.

6. Acknowledgment

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7. Funding

None

8. Competing Interests

The authors declare that they have no competing interests.

Author's Contributions

AH and **AI** designed and preformed the study; they were involved in data collection and also prepared the initial draft of the manuscript in cooperation with **ET**; **AH** and **AI** were also involved in data collection and coordination of clinical, laboratory and other patient data; **ET** was responsible for statistical analysis. All authors have contributed to the discussion and preparation of manuscript draft and have read and approved the final version of it.

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