NON-HODGKIN LYMPHOMA IN PEOPLE LIVING WITH HUMAN IMMUNODEFICIENCY SYNDROME

NE-HOČKINOV LIMFOM KOD LJUDI KOJI ŽIVE SA SINDROMOM STEĆENE IMUNODEFICIJENCIJE

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Summary
Introduction. Even in the era of combined antiretroviral therapy, the mortality rate in patients with human immunodeficiency virus infection remains high, especially with a contributing diagnosis of a malignant disease, such as non-Hodgkin lymphoma. Given the previous, the goal of this research was to establish the incidence of non-Hodgkin lymphoma in human immunodeficiency virus positive patients, as well as to determine their clinical characteristics and mortality in regard to patients with human immunodeficiency virus only. Material and Methods. The retrospective study included 396 human immunodeficiency virus-positive patients. Medical records were reviewed to analyze the average age, duration of infection, average duration of therapy, nCD4+ T-cell count, human immunodeficiency virus viral load, as well as the number and types of malignant diseases. Results. The average age of the patients was 44.2 years; the average nCD4+ T-cell count was 296.94 cells/µL, while the mortality rate was 14.65%. The leading causes of death were non-Hodgkin lymphoma and acquired immunodeficiency syndrome. The most frequently diagnosed malignancy was non-Hodgkin lymphoma, where the average count of nCD4+ T-cells was 162.29 cells/µL. Patients with human immunodeficiency virus and non-Hodgkin lymphoma had significantly lower nCD4+ T-cell count, in regard to patients with human immunodeficiency virus only, and the mortality rate in this group of patients was 85%. Conclusion. The incidence of non-Hodgkin lymphoma in human immunodeficiency virus-positive patients represents a growing threat, given the exceptionally high mortality. The nCD4+ T-cell count may indicate acquired immunodeficiency syndrome and late diagnosis of human immunodeficiency virus together are predictors for non-Hodgkin lymphoma and its poor outcome. It points to the importance of increasing the scope of human immunodeficiency virus testing, as well as finding a better treatment approach.

Key words: Lymphoma, Non-Hodgkin; HIV Infections; Acquired Immunodeficiency Syndrome; Mortality; CD4-Positive T-Lymphocytes; CD4 Lymphocyte Count; Early Diagnosis

Sažetak
Uvod. Uprkos uvođenju kombinovane antiretrovirusne terapije, stopa smrtnosti kod pacijenata sa infekcijom virusom humane imunodeficijencije i dalje je visoka, naročito ukoliko imaju istovremeno dijagnostikovano maligno oboljenje, a posebno ne-Hočkinov limfom. Cilj ovog istraživanja bio je da se utvrdi učestalost ne-Hočkinovog limfoma kod pacijenata pozitivnih na virus humane imunodeficijencije, njihove kliničke karakteristike i smrtnost u odnosu na pacijente bez ne-Hočkinovog limfoma. Materijal i metode. Retrospektivna studija je obuhvatila 396 ispitanika sa potvrđenom infekcijom virusom humane imunodeficijencije. Uvidom u medicinsku dokumentaciju, analizirane su prosečne godine života, prosečna dužina trajanja infekcije i terapije, broj nCD4+ T-limfocita, broj virusnih kopija, kao i broj i vrsta malignih oboljenja. Rezultati. Prosečna starost pacijenata u našoj studiji iznosila je 42, godine, a prosečan broj nCD4+ T-limfocita 296,94 ćelija/µL, dok je stopa smrtnosti bila 14,65%. Vodeći uzroci smrti su bili ne-Hočkinov limfom i sindrom stećene imunodeficijencije. Najučestaliji malignitet bio je takođe ne-Hočkinov limfom, pri čemu je prosečna vrednost nCD4+ T-limfocita u ovoj grupi iznosila 162,29 ćelija/µL. Pokazana je statistički značajna manja vrednost nCD4+ T-limfocita u grupi pacijenata sa infekcijom virusom humane imunodeficijencije i ne-Hočkinovim limfomom u odnosu na pacijente koji su imali samo virus humane imunodeficijencije, pri čemu je smrtnost u ovoj grupi iznosila 85%. Zaključak. Ne-Hočkinov limfom kod pacijenata sa infekcijom virusom humane imunodeficijencije predstavlja sve veći problem, sa obzirom na visoku stopu smrtnosti. Budući da su broj nCD4+ T-limfocita i kasna dijagnoza infekcije virusom humane imunodeficijencije najveći faktori rizika za razvoj ne-Hočkinovog limfoma, neophodno je povećati obim testiranja na virus humane imunodeficijencije, te pronaći adekvatniji pristup u lečenju ovih pacijenata.

Ključne reči: non-Hočkin limfom; HIV infekcije; AIDS; mortalitet; CD4+ T limfociti; CD4 broj limfocita; rana dijagnoza

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**Abbreviations**

HIV – human immunodeficiency virus  
AIDS – acquired immunodeficiency syndrome  
ADI – average duration of infection  
ADT – average duration of therapy  
ART – antiretroviral therapy  
DLBCL – diffuse large B-cell lymphoma  
SPSS – Statistical Package for the Social Sciences  
PLWH – people living with HIV  
NHL – non-Hodgkin lymphoma

**Introduction**

With improvements in antiretroviral therapy (ART), the incidence of acquired immunodeficiency syndrome (AIDS) related opportunistic infections and tumors has decreased. However, the mortality rate in this group of patients remains high [1]. Over the last few decades, many of the most common causes of death in patients with human immunodeficiency virus (HIV) infection have changed its course, and due to ART they became significantly less prominent. However, malignant diseases remain in the focus of interest, considering that they are responsible for the largest number of deaths in HIV-infected patients [2]. Due to the decline in the immune system in HIV-infection, it is comprehensible how these patients are more susceptible to the development of malignant diseases. A large number of recent studies have shown that non-AIDS-defining malignancies are increasingly prevalent in the world, most likely as a result of prolongation of life, thus creating the basis for the onset of comorbidities [3]. Contrary to the previous, in our population AIDS-defining malignancies are highly present and the incidence is still increasing. Among them, the most common is non-Hodgkin lymphoma (NHL), in its three subtypes - diffuse large B-cell (DLBCL), Burkitt, and central nervous system lymphoma. The presumed pathogenic mechanisms for the onset of lymphomas in HIV-infected population imply the effect of oncogenic viruses, excessive secretion of cytokines, as well as chronic antigenic stimulation. Some recent studies also indicate the possible influence of HIV-proteins secreted mostly in germinal centers of lymph nodes, as a contributing factor for the development of lymphomas [4]. As a consequence of immunodeficiency, combined with immune suppression due to chemotherapy, the treatment of these patients is extremely hard and often has a fatal outcome [5]. Several studies have so far identified common characteristics of HIV-positive patients diagnosed with NHL, all relying on the late presentation of HIV as the crucial problem [6, 7]. The goals of this research were to establish the incidence of NHL in this group of patients, determine their immunological parameters and differences compared to HIV-positive patients without NHL in the Autonomous Province of Vojvodina, as well as to determine the most common cause of death in these patients. Given the fact that NHL is AIDS-related malignancy, we hypothesized that patients with HIV and NHL have a significantly lower immune system compared to patients with HIV only. Considering the fact that regular HIV testing is still neglected in our country, we also hypothesized that the majority of patients were diagnosed at a late stage of HIV-infection, and that the most common cause of death in these patients was AIDS-related.

**Material and Methods**

This retrospective study was performed at the Clinic of Infectious Diseases, Clinical Center of Vojvodina, from January 2007 to December 2019. The Ethics Committee of the Clinical Center of Vojvodina has reviewed and approved the study. The study included a total of 396 patients with HIV diagnosis, confirmed by Western-Blot analysis and PCR assay. Patients aged younger than 18 years were excluded. The medical records were reviewed to collect information on demographic, clinical characteristics and laboratory test results. We analyzed the following variables: demographics (age, gender) and clinical (average duration of infection (ADI), average duration of therapy (ADT), nCD4+ T-cell, and HIV viral load

| Table 1. Demographic and clinical characteristics of HIV-infected patients (2007–2019) | Tabela 1. Demografske i kliničke karakteristike pacijenata sa HIV infekcijom (2007–2019) |
|---|---|
| Patients/Pacijenti | N (%)/Broj (%)  |
| Gender/Pol | 396 (100%)  |
| Male/Muški | 364 (91.92%)  |
| Female/Ženski | 32 (8.08%)  |
| Age/Starost | Years/Godine  |
| 42.20  |
| ADI | Months/Meseči  |
| 78.52  |
| ADT | Months/Meseči  |
| 66.23  |
| CD4+ nadir | Min/Minimum  |
| 1  |
| Max/Maksimum | Cells/µL/Ćelije/µL  |
| 1265  |
| Median/Medijana | 296.94  |
| Mortality rate/Stopa smrtnosti | N (%)/Broj (%)  |
| 58 (14.65%)  |

Legend: ADI – average duration of infection, ADT – average duration of therapy

Legenda: ADI – Prosečna dužina trajanja infekcije, ADT – Prosečna dužina trajanja terapije, HIV – virus humane imunodeficijencije
Results

In total, 396 patients (92% male and 8% female) with HIV infection were included in the study, whose mean age was 42.2 years (Table 1). The ADT from 2007 to 2019 was 78.52 months, while the ADT was 66.23 months. The lowest nCD4+ T-cell count was 1, while the highest nCD4+ T-cell count was 1265 cells/µL, respectively. The mortality rate was 14.65% by the end of the study, during the period of 12 years. The leading causes of death were NHL (20.69%) and AIDS (20.69%), followed by pneumonia (13.79%), progressive multifocal leukoencephalopathy (PML) (10.45 months). Among the patients with diagnosed NHL, the lowest viral load was 22101 copies/mL while the highest recorded value was 4199025 copies/mL (mean was 868720.23 copies/mL). The average duration of infection was 62.62 months. Compared to all patients in the study, the ADT for patients with diagnosed NHL was significantly lower (10.45 months). Among the patients with diagnosed NHL, the lowest viral load was 22101 copies/mL while the highest recorded value was 4199025 copies/mL (mean was 868720.23 copies/mL). There was a statistically significant difference in the nCD4+ T-cell count between HIV-positive patients

determined by polymerase chain reaction assay. All diagnoses of malignant diseases were histopathologically confirmed.

Statistical data processing was done using the software program Statistical Package for the Social Sciences (SPSS) version 21.0. The descriptive analysis included calculating mean, minimum, maximum and median values. The normality of the distribution and the homogeneity of the variance were tested for each group, and afterwards difference between variables was determined by Student’s t-test. The values of p < 0.05 were considered statistically significant.

Graph 1. Distribution of patients by cause of death

Legend: NHL – non-Hodgkin lymphoma, PCP – pneumocystis carinii pneumonia, PML – progressive multifocal leukoencephalopathy, AMI – acute myocardial infarction

Legend: DLBCL – diffuse large B-cell lymphoma

Table 2. Distribution of malignant diseases in patients with HIV infection

| Type of malignant disease | AIDS-defining tumors | Non-AIDS-defining tumors |
|---------------------------|----------------------|--------------------------|
| NHL                       | 1 (4.76%)            | 1 (4.76%)                |
| DLBCL                     | 14 (66.67%)          | 21 (100%)                |

All values were calculated relative to a total number of patients

Legend: DLBCL – diffuse large B-cell lymphoma

Legenda: DLBCL – difuzni B-krupnoćelijski limfom, AIDS – sindrom stečene imunodeficijencije, NHL – ne-Hoćkinov limfom

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*All the values were calculated relative to a total number of patients*
and HIV-positive patients with diagnosed NHL – significantly lower nCD4+ T-cell count was present in patients with NHL. In regard to the ADT, there were statistically significant differences between groups. Furthermore, although age, ADI and viral load have been considered as clinical parameters of HIV-positive patients with diagnosed NHL, in our study they were not statistically significant (Table 4).

**Discussion**

The low difference in the ADI and ADT in our study can be explained by changes in 2016 European AIDS Clinical Society (EACS) guidelines, which recommend starting combined antiretroviral therapy (cART) as soon as possible, irrespectively of CD4 T-cell count [8]. Analyzing the clinical characteristics of patients with HIV infection, we found that the average count of nCD4+ T-cell was 296.94 cells/µL. Given the fact that nadir CD4+ T-cell count below 300 cells/µL represents AIDS, this result speaks in favor of the fact that the majority of HIV-positive patients are diagnosed at a late stage of infection, which confirmed our hypothesis. Recent studies have also shown that over 50%

**Table 3.** Characteristics of patients with HIV infection and NHL diagnosis

| Parameter/Parametar | Mean/Srednja vrednost | p* |
|---------------------|-----------------------|----|
| Age (PLWH)/Starost (HIV-poziitivni pacijenti) | 42.01 | 0.0569 |
| Age (PLWH+NHL)/Starost (HIV+NHL) | 48.09 | |
| nCD4+ T-cells count (PLWH)/broj nCD4+ ćelija (HIV) | 300.15 | 0.0047 |
| nCD4+ T-cells count (PLWH+NHL)/broj nCD4+ T-ćelija (PLWH+NHL) | 162.29 | |
| ADI (PLWH) | 79.08 | 0.5555 |
| ADI (PLWH+NHL) | 62.62 | |
| ADT (PLWH) | 67.94 | |
| ADT (PLWH+NHL) | 10.45 | |
| Viral load (PLWH)/Broj kopija virusa (HIV) | 924524.61 | 0.9105 |
| Viral load (PLWH+NHL)/Broj kopija virusa (HIV+NHL) | 868720.23 | |

\* p < 0.05 was considered statistically significant. **p < 0.05 je smatrano statistički značajno**

Legend: ADI – average duration of infection, ADT – average duration of therapy, PLWN – people living with HIV, NHL – ne-Hočkinov limfoma, PLWH – osobe sa infekcijom virusom humane imunodeficijencije.
of all HIV diagnoses were established at a late stages of infection [9, 10]. This result indicates the need to increase the extent and frequency of HIV-testing, especially in populations at high risk for this infection, in order to prevent AIDS-related complications. The mortality rate in our study was 14.65%, and the most common causes of death were non-Hodgkin lymphoma and AIDS. A number of studies have shown that despite highly effective ART, the incidence and number of deaths caused by NHL in people living with HIV (PLWH) is still increasing. For example, a study in the United States showed that among patients with NHL, especially DLBCL, the highest mortality was found in the group of patients with conjoint HIV-infection. The fact that DLBCL is one the most frequent B-cell lymphomas in PLWH, with high mortality, was also confirmed in a German cohort study with overall death rate higher than 30%, as well as in the study in Sub-Saharan Africa, where patients with HIV and NHL had a poor survival [11–13]. The assumed reason for this lies in severe immunodeficiency combined with immunosuppression in these patients, and therefore, a very complicated treatment and a specific approach are needed. Besson et al. reported that the mortality rate of patients with NHL does not change regarding whether they have HIV or not, however, the rate of NHL recurrence in HIV patients is significantly higher in regard to non-HIV populations [14]. Equal number of patients in our groups died from AIDS. The exact cause of death in this group of patients could not be established, due to the fact that they all died before being diagnosed with an AIDS-related condition. AIDS has also been confirmed as one of the most common causes of death in studies done in Asia and Canada [15, 16]. Non-AIDS defining malignancies were the least common cause of death in our study. These results differ from many recent studies in which malignancies not related with AIDS are the first or second most common cause of death in PLWH [17, 18]. In those studies, patients were diagnosed mostly in early stages of HIV infection, therefore they had a better chance for immune reconstitution, hence life prolongation, unlike patients in our study. This result again implicates the necessity of more extensive testing for HIV in our population in order to obtain early diagnosis. Considering the pathogenesis of HIV infection that leads to slow destruction of the immune system, it is understandable how these patients are more susceptible for developing a malignant disease. Therefore, it is expected that in the analysis of the prevalence of malignant diseases, non-Hodgkin lymphoma is in the first place. The second most common malignant disease was Kaposi's sarcoma accounting for 24%, while non-AIDS malignancies accounted only for 9%. The introduction of cART at the beginning and its constant improvement has led to better outcomes of many malignant diseases, as well as other AIDS-related comorbidities. However, due to a rising number of complications and lethal outcomes of patients with NHL and HIV, a number of studies have been conducted to determine the incidence and characteristics of these patients, all confirming very high incidence of NHL in HIV positive patients. Our results speak in favor of increasing NHL incidence in PLWH over time, as confirmed by Howlader, Olszewski and Ramaswamii [11, 19, 20]. The question that remains is whether this increase is attributable to a real increase in incidence, or just higher HIV testing frequency in people with NHL, since it has not been a consistent practice until recently. Speaking of the factors that may contribute to the development of NHL in HIV-positive patients, we found that detection of late-stage HIV infection is one of the most significant factors. The average number of nCD4+ T-cells count in patients with NHL and HIV in our study was 162.29 cells/µL, far below the limit for the diagnosis of AIDS, whereby their count of nCD4+ T-cells was significantly lower in relation to the count of these cells in patients without NHL. The fact that the diagnosis of AIDS according to nCD4+ T-cell count is a strong predictor for NHL was confirmed in other studies as well [14, 19, 21–23]. Taking into consideration the fact that nCD4+ T-cells count is an indirect indicator of infection duration, this result was expected. Most of the patients in our study were diagnosed with AIDS and NHL at the same time, with mortality rate of 85%. Already existing immune deficiency in these patients due to HIV infection, with further immune suppression due to chemotherapy for NHL explain how the combination of these two conditions suggest poor outcome, as indicated in other studies as well [23–25]. Most of these patients died soon after diagnosing AIDS and NHL, which is why the ADI and therapy in these patients differ in regard to patients with HIV, and why they have statistically lower duration of therapy in comparison with HIV-positive patients only. Even though Hentrich and Howlader suggested that one of the contributing factors for the onset of NHL is older age, in our study we have not found a statistically significant difference between PLWH without and with NHL, but the difference is almost significant [12, 14]. This can be explained by the fact that the general population in our study was older, as well as the fact that patients with HIV and NHL died before finishing the study and calculation of the overall age of patients.

Conclusion

Even though combined antiretroviral therapy has changed the course of human immunodeficiency virus infection, the mortality rate in these patients remains high. In the Autonomous Province of Vojvodina, the most common causes of death are acquired immunodeficiency syndrome related conditions, due to insufficient scope of human immunodeficiency virus testing. As one of the most common causes of death, and also one of the most common malignant diseases, non-Hodgkin lymphoma is a growing threat. Late diagnosis of human immunodeficiency virus and CD4+ T-cell count indicative for acquired immunodeficiency syndrome are predictors of non-Hodgkin lymphoma and poor outcome. Increasing the scope of human immunodeficiency virus testing should contribute to earlier diagnosis of human immunodeficiency virus,
and therefore better outcome for these patients. In addition, even though we did not have a representative sample in our study, improvement in the field of screening for non-human immunodeficiency virus related malignancies should be in the focus of interest, as suggested in a number of researches done so far.

References

1. Gingo MR, Nouria M, Kessinger CJ, Greenblatt RM, Huang L, Kleerup EC, et al. Decreased lung function and all-cause mortality in HIV-infected individuals. Ann Am Thorac Soc. 2018;15(2):192-9.

2. Jasra S, Kazemi M, Cole D, Acuna-Villaorduna A, Mantzaris I, Shastri A, et al. Causes and predictors of early mortality in HIV-positive and HIV-negative patients with diffuse large B-cell lymphoma. Blood. 2018;132(Suppl 1):1713.

3. Dalla Pria A, Bower M. AIDS-related malignant disease. Med. 2018;46(6):365-9.

4. Dolcetti R, Gloghini A, Caruso A, Carbone A. A lymphomagenic role for HIV beyond immune suppression? Blood. 2016;127(11):1403-09.

5. Shiels MS, Engels EA. Evolving epidemiology of HIV-associated malignancies. Curr Opin HIV AIDS. 2017;12(1):6-11.

6. Rohner E, Bütkofe L, Schmidlin K, Sengayi M, Maskew M, Giggy J, et al. Non-Hodgkin lymphoma risk in adults living with HIV across five continents. AIDS. 2018;32(18):2777-86.

7. Sigel K, Park L, Justice A. HIV and cancer in the Veterans Health Administration System. Semin Oncol. 2019;46(4-5):334-40.

8. European AIDS Clinical Society. Guidelines v10.0 November 2019 [monograph on the Internet]. EACS European AIDS Clinical Society; 2019 [cited 2020 Feb 9]. Available from: https://www.eacsociety.org/files/2019_guidelines-10.0_final.pdf.

9. Mojmidar K, Vajpayee M, Chauhan NK, Mendiratta S, Singh S, Singh S, et al. AIDS-related malignant disease. J Exp Med. 2018;244(3):231-42.

10. Camoni L, Raimondo M, Regine V, Salfa MC, Suligoi B. Late presenters to HIV care and treatment, identification of associated risk factors in HIV-1 infected Indian population. BMC Public Health. 2010;10:416.

11. Howlader N, Shiels MS, Mariotto AB, Engels EA. Contributions of HIV to non-Hodgkin lymphoma mortality trends in the United States. Cancer Epidemiol Biomarkers Prev. 2016;25(9):1289-96.

12. Hentrich M, Wyen C, Gillor D, Mueller M, Stoehr A, Schulze A, et al. Lymphoma-associated mortality in the German HIV-lymphoma cohort study. J Clin Oncol. 2016;34(15 Suppl):7550.

13. Menon M, Coghill A, Mutyaba I, Okuku F, Phipps W, Harlan J, et al. Whom to treat? Factors associated with chemotherapy recommendations and outcomes among patients with NHL at the Uganda Cancer Institute. PloS One. 2018;13(2):e0191967.

14. Besson C, Lancar R, Prevot S, Algarte-Genin M, Delobel P, Bonnet F, et al. Outcomes for HIV-associated diffuse large B-cell lymphoma in the modern combined antiretroviral therapy era. AIDS. 2017;31(18):2493-501.

15. Bzik J, Jiamasakul A, Uy E, Kumarasamy N, Ditango R, Chaiwarith R, et al. Cardiovascular disease-related mortality and factors associated with cardiovascular events in the TREAT Asia HIV Observational Database (TAHOD). HIV Med. 2019;20(3):183-91.

16. Kaida A, Gormley R, Webster K, Carter A, Nicholson V, Wang L, et al. High mortality among women living with HIV enrolled in Canada’s largest community-based cohort study. J Int AIDS Soc. 2018;21:75.

17. Thrift AP, Chiao EY. Are non-HIV malignancies increased in the HIV-infected population? Curr Infect Dis Rep. 2018;20(8):22.

18. Totonchy J, Cesarman E. Does persistent HIV replication explain continued lymphoma incidence in the era of effective antiretroviral therapy? Curr Opin Virol. 2016;20:71-7.

19. Olszewski AJ, Castillo JJ. Outcomes of HIV-associated Hodgkin lymphoma in the era of antiretroviral therapy. AIDS. 2016;30(5):787-96.

20. Ramaswami R, Pria A, Roe J, Nelson M, Gazzard B, Bower M, et al. Evolution of HIV-associated lymphoma over three decades. HIV Med. 2016;17(Suppl 1):1-44.

21. Rabkin CS, Goedert JJ. Chronic hepatitis and non-Hodgkin lymphoma among people with HIV: implications for screening, treatment, and prevention. Ann Intern Med. 2017;166(6):69-70.

22. Pang W, Shang P, Li Q, Xu J, Bi L, Zhong J, et al. Prevalence of opportunistic infections and causes of death among hospitalized HIV-infected patients in Sichuan, China. Tohoku J Exp Med. 2018;244(3):231-42.

23. Aydin OA, Gunduz AT, Sargin F, Mete B, Karaozanoglu HK, Sevgi DY, et al. Prevalence and mortality of cancer among HIV/AIDS patients: a large-scale cohort study in Turkey. East Mediterr Health J. In press. DOI: https://doi.org/10.26719/emhj.19.030.

24. Oprea C, Ianache I, Ionescu P, Calistru P. Malignancies in HIV-infected patients—incidence and predictors of survival in a Romanian health care facility. Romanian Journal of Legal Medicine. 2017;25(2):227-34.

25. Poorolalaj J, Hooshmand E, Mahjub H, Esmaeinasab N, Jenabi E. Survival rate of AIDS disease and mortality in HIV-infected patients: a meta-analysis. Public Health. 2016;139:3-12.