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ORIGINAL PAPER

THE GLOBAL WELL-BEING OF PATIENTS WITH NON-HODGKIN LYMPHOMAS

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Abstract

Introduction. Non-Hodgkin lymphoma (NHL) is a lymphoid tumour with impact of physical health, psychological, spiritual well-being, social integration, the life-disease relationship being thus a multidimensional one.
The objective of the study was to assess the global well-being in patients with NHL.
Material and methods. A descriptive study of 116 adult patients (65 women, 51 men) with NHL was conducted. The individual interview was carried out following an epidemiological, clinical and psychological global well-beeing survey (GWB).
Results. The average GWB score was lower in patients in the age category of 18-40 years (average score 43.75), was higher in men (62.2, moderate distress), which indicates a lower psycho-emotional stress compared to women (54.5, severe distress). Patients with an aggressive NHL reported a significantly lower GWB score (p=0.003). Extranodal disease (p=0.15) and stage of lymphoma (p=0.3) were not statistically significant correlated with the GWB scores. At the end of the first-line treatment of NHL, most patients presented with a positive well-being score (76, 65.6%).

Résumé

Le bien-être global des patients atteints de lymphomes non hodgkiniens

Introduction. Le lymphome non hodgkinien (LNH) est une tumeur lymphoïde ayant un impact sur la santé physique, psychologique, le spirituel bien-être, l'intégration sociale, la relation vie-maladie étant ainsi multidimensionnelle.
L'objectif de l'étude était d'évaluer le bien-être global des patients atteints de LNH.
Materiel et méthodes. L'étude descriptive de 116 patients adultes (65 femmes, 51 hommes) atteints de LNH a été menée. L'entretien individuel a été réalisé suite à une enquête de bien-être épidémiologique, clinique et psychologique (GWB).
Résultats. La moyenne du score GWB était plus faible chez les patients du groupe d'âge 18-40 ans (score moyen 43,75), était plus élevée chez les hommes (62,2, détresse modérée), ce qui exprime moins de stress psycho-émotionnel par rapport aux femmes (54,5, sévère détresse). Les patients atteints d'un LNH agressif ont rapporté un score GWB significativement plus faible (p = 0,003). La maladie extra ganglionnaire (p = 0,15)

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Conclusions. The most vulnerable for the development of severe distress are the younger patients, the female gender, and patients with aggressive NHL. The stage and location of disease onset do not have a direct impact on the well-being of patients with NHL. There is a tendency to improve the well-being after the first-line treatment.

Keywords: non-Hodgkin lymphoma, well-being, score.

List of abbreviations:
NHL – non-Hodgkin lymphoma
GWB – global well-being

et le stade du lymphome (p = 0,3) n'étaient pas statistiquement significatifs associés avec les scores GWB. À la fin du traitement de première intention du LNH, la plupart des patients présentaient un score de bien-être positif (76, 65,6%).
Conclusions. Les plus vulnérables au développement d'une détresse sévère sont les patients plus jeunes, de sexe féminin et atteints d'un LNH agressif. Le stade et le lieu d'apparition de la maladie n'ont pas d'impact direct sur le bien-être des patients atteints de LNH. Il existe une tendance à l'amélioration du bien-être après la première ligne de traitement.

Mots-clés: lymphome non hodgkinien, bien-être, score.

Introduction

Non-Hodgkin's lymphoma (NHL) is a group of hematologic malignancies with increasing morbidity worldwide and in the Republic of Moldova[1,2]. NHL represent approximately 3% of all cancers, and are the most common malignant hemopathies recorded worldwide[3]. In the Republic of Moldova, hematologic malignancies occupy the 5th position as prevalence, after colon, breast, skin (non-melanoma) and lung cancer[4].

The impact of cancer on patients manifests not only from the point of view of physical health, but also of psychological and spiritual well-being, social integration, the life-disease relationship being thus a multidimensional one[5]. Establishing an oncological diagnosis, regardless of its type, is perceived as a traumatic event in life. This fact is conditioned by the multitude of problems not only physical (asthenia, alopecia), but also psychological (depression, anxiety), social (stigmatization), spiritual (loss of meaning) and especially practical (financial problems, absence from work) which considerably influence the quality of life[6]. The psychological reaction to the diagnosis of NHL and its specific treatment reflects the subjective perception of the disease through the perception of changes associated with this disease, changes in family ties[7]. With increasing numbers of long-term lymphoma survivors, there has been a focus on optimizing quality of life, psychological well-being and identifying survivorship challenges[8]. The increase in overall NHL survival rates has been largely attributed to progress in several treatment trials and the application of relevant research findings[9]. The response to treatment and patient survival did not reflect data about psychological and emotional well-being of the patient with NHL[10,11].

The global well-being of patients diagnosed with cancer has a major impact not only on the diagnosed patients, but also on social relationships with friends, work colleagues and family relationships[12]. The indicators of psychological well-being and quality of life vary from the stage of cancer diagnosis to survivorship, although some physical, social and emotional effects may be persistent[8,13]. The impact of the uncertainty regarding the prognosis, physical condition and side effects of the treatment, the fear of death on the psychological and emotional state are evaluated especially initially, during the period of suspicion of oncological diagnosis, and then during the treatment[14]. The fear of relapse or progression of the disease alters the psycho-emotional well-being even after finishing the treatment with achievement of complete remission[15]. Patients with lymphoma have improved survival rates in recent years[16]. Lymphoma patients are younger than most other cancer patients. When a cancer diagnosis is given, the identification of groups at risk of severe deterioration of well-being is very important[17]. Incorporating patient-reported outcomes allows recognition of factors that significantly influence the degree of psychological distress in NHL patients. A better understanding of issues related to psychological well-being generates impetus for changing practice, improving education and designing behavioral interventions. In this context, we conducted this first study in the Republic of Moldova to evaluate the well-being of patients with NHL, before and after the first-line chemo-immunotherapy.

The objective of our study was to assess the global well-being of NHL patients.

Material and methods

The study included 116 patients with aggressive and indolent NHLs hospitalized in the Hematology Department of the Oncological Institute, Chisinau,

Republic of Moldova, between February 2020 and February 2021: 65 women, 51 men. The criteria for inclusion in the study were patients' age over 18 years, with histologically confirmed NHL, and patient's agreement to participate in the study. The exclusion criteria were age less than 18 years, patient's disagreement to participate in the study. The diagnosis of NHL was established according to the 2016 revision of the World Health Organization classification of lymphoid neoplasms[18]. The lymphoma stage was established according to Ann Arbor staging system[19].

The individual interview was carried out following an epidemiological survey (gender, ages, living environment), a clinical survey (NHL type, Ann Arbor stage, onset of the disease) and a survey on psychological well-being (scoring/interpretation GWB; there is a total score running from 0 to 110, with lower scores indicating more severe distress). The three levels of distress are divided accordingly: 0 to 60 reflect "severe distress"; 61 to 72 ,"moderate distress"; and 73 to 110 "positive well-being". The completion of the survey required approximately 10-15 minutes. The GWB score includes positive and negative questions in 6 dimensions: well-being, self-control, depression, vitality, anxiety, and general health. Each item has the time range "during the last month" and the first 14 questions use 6-point response scales representing intensity or frequency. The other 4 questions use 0-10 rating scales. The polarity of items 1, 3, 6, 7, 9, 11, 15, and 16 is reversed for scoring, and items from each subscale are summed together for a total score. Lower scores reflect distress and higher scores reflect positive well-being[20].

Descriptive statistics were used to characterize the study group. The difference between pre- and posttreatment GWB score was evaluated using the paired t-test. Univariate linear regression was used to assess the association between the initial GWB score and clinical factors (age, gender, residence, NHL type, stage, presence of extranodal manifestations). Independent variables were then included in a multivariate linear regression model. Statistical analyses were conducted using the Graphpad Prism ver. 9.3.0 software. Two-tailed p-values were used, and statistical significance was considered at $p < 0.05$.

This study was approved by the ethics committee of the State University of Medicine and Pharmacy "Nicolae Testemitanu", Chisinau, Republic of Moldova, January 28th, 2020, session nr. 32.

Results

According to the inclusion criteria, 116 new NHLs patients were included in study and able to complete the survey before and after the first-line chemo-immunotherapy for lymphoma. The general characteristics and the corresponding GWB scores of the study subjects are presented in Table 1.

Table 1. The general characteristics of the patients and GWB score.

Criteria		*Patients (%)*	*Mean GWB score*
Age	18-30	4 (3.4)	43.75
	31-40	9 (7.8)	48.4
	41-50	20 (17.2)	62.8
	51-60	36 (31.0)	63.3
	61-70	32 (27.6)	56.1
	71+	15 (12.9)	51.4
Gender	M	51 (44.0)	62.2
	F	65 (56.0)	54.5
Stage	I	8 (6.9)	55.7
	II	25 (21.6)	
	III	20 (17.2)	58.8
	IV	63 (54.3)	
Lymphoma subtype	Indolent	49 (42.2)	62.4
	Aggressive	67 (57.8)	54.6
Extranodal sites	Absent	79 (68.1)	59.2
	Present	37 (31.9)	55.1

GWB, general well-being

The median patient age was 58.5 (IQR 47, 64). Most commonly, NHL developed in patients in the age group of 51-60 years (36.31%), followed by patients aged 61-70 years (32 patients, 27.6%). Much less often NHL have developed in people aged between 41-50 years (20 patients, 17.2%) and over 70 years of age (15 patients, 12.9%). Rarely, NHL has been diagnosed in the age groups of 31-40 years (9 patients, 7.8%) and 18-30 years (4 patients, 3.4%). The distribution of *de novo* patients with NHL according to the mean of the GWB score demonstrates the development of severe distress predominantly in patients in the age category of 18-40 years and over 61 years old. Although only 4 (3.4%) patients included in our study were aged 18-30 years, they had the lowest score of the GWB scale (43.75), respectively they are the most vulnerable for the development of severe distress. Patients aged 41-60 years, according to the results of the survey, accumulated an average score of the GWB scale of 63.05 (moderate distress). While older age seemed to be associated with a higher GWB score, in a univariate linear regression analysis, age was not statistically significant associated with the GWB scores (p=0.82).

Out of 116 patients, 65 (56%) were female and 51 (44%) were male. The average GWB score was higher in men (62.2, moderate distress), which indicates less

Table 2. The GWB score before and after treatment.

	Pre-treatment GWB	*Post-treatment GWB*
Mean (95% CI)	57.9 (55.3-60.5)	80.7 (77.7-83.6)
Median (IQR)	56 (47.5, 67.0)	81.5 (70.0, 94.8)
Range	32-98	35-110
Grouped scores (n, %)		
Severe distress	74 (63.8)	19 (16.4)
Moderate distress	28 (24.1)	21 (18.1)
Positive well-being	14 (12.1)	76 (65.6)

GWB, general well-being; IQR, interquartile range

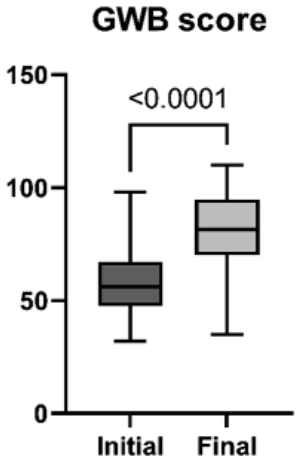


Figure 1. The mean difference between pre- and post-treatment GWB score.

psychoemotional stress compared to women (54.5, severe distress). The male gender positively correlated with a higher GWB score (p=0.004).

With respect to the NHL subtype, 67 (57.8%) subjects were classified as having an aggressive histological type, and 49 (42.2%) had an indolent lymphoma. Patients who presented with an aggressive NHL reported a significantly lower GWB score (p=0.003). In a multivariate model, gender and NHL subtype had statistical significance.

Most participants did not have any extranodal onset of disease (79 patients, 68.1%). In a univariate linear regression analysis, the presence of extranodal disease (p=0.15) was not statistically significant for an association with the GWB scores.

Most of the patients presented with advanced (III-IV) disease stage (83 patients, 71.5%), mainly stage IV (63 patients, 54.3%). The minority had limited stage (I-II) lymphoma (33 patients, 28.5%), mainly stage II (25 patients, 21.6%). The distribution of patients with NHL, according to the degree of dissemination of the tumour and the average score of the GWB scale, shows the lack of an obvious difference between the level of distress and the stage of the disease. Both in the earliest stages (I, II) and in the advanced stages (III, IV), the level of distress was recorded without significant statistical differences (55.7 and 58.8 average GWB score, respectively). Statistical analysis showed that, in a univariate linear regression analysis, the stage of lymphoma was not statistically significant for an association with the GWB scores (p=0.3).

Table 2 contains the GWB scores pre- and post-treatment. In total, during pre-treatment most patients presented with a severe distress level (74 patients, 63.8%); 28 patients (24.1%) had a moderate distress level, and only 14 patients (12.1%) were considered to have a positive well-being score.

At the end of the first-line treatment of NHL, a change in the frequency of distress states was observed. Most patients presented with a positive well-being score (76 patients, 65.6%). As expected, specific treatment had a significant effect on the general well-being. In this study, the mean GWB score among lymphoma patients was 57.9 (95% CI 55.3-60.5) with a range of 32-98 before treatment initiation. After therapy for NHL, the mean GWB score was 80.7 (95% CI 77.7-83.6), with a range of 35-110.

The mean difference between pre- and post-treatment score was 22.8 (95% CI 19.6-26.0), which was statistically significant (p<0.0001) (Figure 1).

Discussion

According to the research published by Perz and co-authors, in which they reflect the analysis of distress in patients diagnosed with different types of cancer, the prevalence of oncological distress varies depending on the type of cancer, stage of the disease, and patient's age or gender[21]. Based on the results of our research, we found that people in the age group 18-40 years and elderly people confirmed with NHL are the most vulnerable to severe distress. However, the age of patients included in the study did not correlate statistically significant with GWB score. The same conclusion was formulated following the study of psycho-emotional distress in 456 patients with lymphoma in the Netherlands[22]. The authors concluded that younger patients experienced more psychological distress. This was explained by young patients with NHL experiencing multiple problems, for example due to stress caused by loss of fertility, health care expenses, childcare,

absence from work because of cancer treatment or side effects, and lack of financial or work stability[23]. Therefore, they may be more vulnerable to psychological distress compared to older patients.

Knowledge about the psychological processes and effects of gender differences among cancer patients is lacking[24,25]. Our study demonstrates a statistically significant correlation of male gender with the GWB score. Women have higher vulnerability and require psychological support during the entire route from diagnosis to finishing the first-line treatment of NHL. According to the study by Matthews et al., women with cancer report higher rates of distress than men, with cancer-related anxiety, fear of cancer recurrence, worry about diagnostic tests, and uncertainty about future[26]. In the case of malignant hemopathies, gender differences have a different interpretation, with female patients showing more symptoms and greater overall distress from the disease compared to male patients in Pandey's study[27]. Cole et al. observed that women were more likely to have a history of depression than men[28]. More recently, Bergerot et al. findings suggest that gender differences were related to distress, but not to neoplasm grade, and in particular women reported more distress, anxiety, and depression than male patients[29]. However, there is little understanding of the mechanisms underlying these gender differences.

As previously shown, our study included patients who developed different types of NHL classified as aggressive and indolent. The clinical presentation of aggressive B- and T-cell lymphomas may include rapidly growing masses, B symptoms (high fever – 38°C or higher, weight loss of a tenth or more of the previous weight over the past 6 months, night sweats)[30]. The general condition of patients who develop aggressive NHL is more altered, the treatment applied is more intensive, which reflect directly on the well-being. Our study demonstrated that patients with aggressive NHLs reported a significantly lower GWB score (p=0.003) and are vulnerable to develop oncological distress. The same results were obtained by Wagner et al., with the finding of a higher level of anxiety and altered quality of life in patients with aggressive NHL as opposed to those with indolent NHL[31]. Regardless of the NHL stage and location of the primary tumour, the patients included in the study developed a high level of psycho-emotional stress.

According to the literature review, the assessment of well-being of survivors was most frequently done at intervals of months or years[32,33]. We aimed to evaluate the well-being of the patient with NHL immediately upon finishing the first-line treatment and we obtained that most patients presented with a positive well-being score.

The information obtained from the patient by using this questionnaire, although subjective, is important when making decisions about therapeutic management. This study had several limitations. Although information was available regarding the characteristics of nonrespondents, it remains unknown why they declined to participate. This perhaps resulted in a small selection bias. Our study demonstrates the importance of evaluating the GWB as soon as the patient is informed about the cancer diagnosis.

Conclusions

The most vulnerable for the development of severe distress are patients of younger age, female gender and those with aggressive NHL. The stage and location of disease onset (nodal or extranodal) do not have a direct impact on the well-being of patients with NHL. In this study, there was a tendency to improve well-being after the first-line of treatment.

Author Contributions:

Conceptualization, S.B. and M.M.; methodology, L.M-N.; software, V.T. and I.N.; validation, M.M. and M.R.; formal analysis, S.B.; investigation, S.B. and M.M.; resources, S.B.; data curation, S.B. and M.M.; writing–original draft preparation, S.B.; writing–review and editing, M.M, S.B., M.R., V.T.; visualization, M.R. and L.M-N.; supervision, M.M.; project administration, M.M. All the authors have read and agreed with the final version of the article.

Compliance with Ethics Requirements:

"The authors declare no conflict of interest regarding this article"

"The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study"

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References

1. Perry A, Diebold J, Nathwani B, et al. Non-Hodgkin lymphoma in the developing world: Review of 4539 cases from the international Non-Hodgkin Lymphoma Classification Project. *Haematologica*. 2016; 101(10):1244-1250.
2. Buruiana S. Clinical, hematologic, and immunohistochemical aspects of small lymphocytic non-Hodgkin's lymphomas. *INFO-MED*. 2016; 2(28):52-58.

3. Thandra KC, Barsouk A, Saginala K, Padala SA, Barsouk A, Rawla P. Epidemiology of non-Hodgkin's lymphoma. *Medical Sciences (Basel, Switzerland).* 2021;9(1):5.
4. www.onco.md (Accessed on January 21, 2023).
5. Mihoc R, Pustianu V, Degi L. Psycho-oncology in Romania. New perspectives and research directions. *Romanian Journal of Medical Practice*. 2021; 16(1):49-54.
6. Cordova MJ, Riba MB, Spiegel D. Post-traumatic stress disorder and cancer. *Lancet Psychiatry.* 2017;4(4):330-338.
7. Cara O, Calancea V. Addressing psychoemotional disorders in oncology patients. *Psychology.* 2022;2(41):71-82.
8. Rosenthal A. Quality of life and survivorship in lymphoma. *Current Oncology Reports*. 2022; 24:1113–1120.
9. Mejia M, Perez A., Watson H, et al. Successful treatment of severe type B lactic acidosis in a patient with HIV/AIDS-associated high-grade NHL. *Case Reports Immunology.* 2018; 2018:9093623.
10. Buruiana S, Robu M, Mazur-Nicorici L, Tomacinschii V, Mazur M. Assessing the quality of life in patients with non-Hodgkin's lymphoma is a burden or an advantage? *Arch Balk Med Union*. 2020; 55(3):418–424.
11. Papadopulus D. The role of well-being, spirituality and religiosity for successful aging in later life: a brief review. *Advances in Aging Research*. 2020; 9(2):23-32.
12. Riaz S, Anjum R, Akram B, et al. Psychological wellbeing scale for cancer patients: revised version. *Pakistan Armed Forces Medical Journal*. 2020; 70 (4): 1125-32.
13. Buruiana S. The importance of the psyho-spiritual state of patients with non-Hodgkin's lymphoma. *European Journal of Biomedical and Life Sciences.* 2020; 4:37-39.
14. Mehnert A, Hartung TJ, Friedrich M, et al. One in two cancer patients is significantlydistressed: Prevalence and indicators ofdistress. *Psycho-Oncology*. 2018; 27(1):75-82.
15. Soleimani MA, Bahrami N, Allen KA, Alimoradi Z. Death anxiety in patients withcancer: A systematic review and meta-analysis. *The European Journal of Oncology Nursing.* 2020; 48:101803.
16. Miller KD, Nogueira L, Mariotto AB, et al. Cancer treatment and survivorship statistics, 2019. *CA: A Cancer Journal for Clinicians*. 2019; 69(5):363-385.
17. International Society for Traumatic Stress Studies/ISTSS. Posttraumatic Stress Disorder Prevention and Treatment Guidelines. Methodology and Recommendations (https://istss.org/getattachment/Treating-Trauma/New-ISTSS-Prevention-and-Treatment. (Accessed December 10th, 2022).
18. Swerdlow SH, Campo E, Harris NL, et al, J. (Eds.) WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, Revised 4th ed.; IARC: Lyon, France, 2017.
19. Armitaje G. Staging non-Hodgkin lymphoma. *Cancer Journal for Clinicians*. 2005; 55:368–376.
20. Anglim J, Horwood S, Smillie L, et al. Predicting psychological and subjective well-being from personality: A meta-analysis. *Psychological Bulletin*. 2020; 146(4), 279–323.
21. Perz J, Ussher JM, Butow P, Wain G. Gender differences in cancer carerpsychological distress: an analysis ofmoderators and mediators. *European Journal Cancer Care (Engl).* 2011; 20(5):610-9.
22. Lindy PJ, Oerlemans S, Schoormans D, et al. Psychological distress among patients with lymphoma: the association with personality and coping strategies. *Journal of Psychosocial Oncology Research and Practice*. 2021; 3(1):p e041.
23. Banegas MP, Schneider JL, Firemark AJ, et al. The social and economic toll of cancer survivorship: a complex web of financial sacrifice. *Journal of Cancer Survivorship*. 2019; 13:406–417.
24. Hinz A, Herzberg PY, Lordick F, et al. Age and gender differences in anxiety and depression in cancer patients compared with the general population. *European Journal of Cancer Care (English).* 2019; 28, e13129.
25. Koyama A, Matsuoka H, Ohtake Y, et al. Gender differences in cancer-related distress in Japan: a retrospective observation study. *Biopsychosocial Medicine*. 2016; 10. https://doi.org/10.1186/s13030-016-0062-8.
26. Matthews BA. Role and gender differences in cancer-related distress: a comparison of survivor and caregiver self-reports. *Oncology Nursing Forum.* 2003; 30(3):493-9.
27. Pandey M, Sarita GP, Devi N, et al. Distress, anxiety, and depression in cancer patients undergoing chemotherapy. *World Journal of Surgical Oncology*. 2006; 4, 68–72.
28. Cole CE, Haugen AR, Mathiason MA, McHugh VL. Screening for psychosocial distress in patients with hematological malignancies and identifying specific factors that cause distress throughout stage disease. *Blood*. 2011;118: 2086.
29. Bergerot CD, Clark KL, Nonino A, Waliany S, Buso MM, Loscalzo M. Course of distress, anxiety, and depression in hematological cancer patients: Association between gender and grade of neoplasm. *Palliative Supportive Care*. 2015; 13: 115-123.
30. Fenske T, Kapke JT. Aggressive Lymphoma. In: Lazarus, H., Schmaier, A. (eds) Concise Guide to Hematology. Springer, Cham. 2019; https://doi.org/10.1007/978-3-319-97873-4_32.
31. Wagner LI, Zhao F, Hong F, et al. Anxiety and health-related quality of life among patients with low-tumor burden non-Hodgkin lymphoma randomly assigned to two different rituximab dosing regimens: results from ECOG trial E4402 (RESORT). *Journal of Clinical Oncology*. 2015; 33(7):740-8.
32. Perez G, Walsh E, Quain K, Abramson J, Park E. A virtual resiliency program for lymphoma survivors: helping survivors cope with post-treatment challenges. *Psychology & Health*. 2021; 36(11): 1352-1367.
33. Hackett F, Dowling M. Lymphoma survivors' experiences at the end of treatment. *Journal of Clinical Nursing.* 2019; 28(3–4): 400–409.