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ORIGINAL ARTICLE

Retrospective Analysis of Prognostic Factors in Pediatric Hodgkin Lymphoma

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OBJECTIVE

To examine the treatment outcomes and prognostic factors influencing the results in patients treated for pediatric Hodgkin lymphoma.

METHODS

The study included 115 pediatric patients treated for Hodgkin lymphoma at our clinic between 2007 and 2024. The patients' demographic data, age at diagnosis, disease stage, presenting symptoms, outcome, complete blood count parameters, and positron emission tomography (PET) results were retrospectively reviewed from their medical records.

RESULTS

The mean age at diagnosis for the 115 patients included in the study was 12.3±4 years (Range: 2–18 Years). Of the cases, 45.2% (n=52) were female and 54.8% (n=63) were male. Among complete blood count parameters, the mean hemoglobin level was 11.16±1.6 g/dL (Range: 7–16). Anemia was more frequently observed in patients with advanced-stage disease (p=0.04). The frequency of B symptoms differed significantly in patients with anemia (p=0.03). Although relapse was more frequently observed in this group, no statistically significant difference was found compared to the other group. Examination of PET results at the end of treatment revealed PET negativity in 59.1% (n=68) of patients, progressive/refractory disease in 7% (n=8), and partial PET response in 6.1% (n=7). During follow-up, relapse/refractory disease was observed in 16.5% (n=19) of patients. The mean age of patients with relapse was higher (14 vs. 11.9). In the relapse group, leukocyte counts were higher, hemoglobin levels were lower, and platelet counts were significantly higher compared to the other group. In addition, erythrocyte sedimentation rate was higher (p=0.039), and the frequency of B symptoms was greater (p=0.001) in this group. The mean follow-up period was 90±52 months (6–200), and 8.7% (n=10) of patients died during follow-up. Six patients died due to infection, pneumonia, or respiratory failure, and four died due to disease progression. The mean survival time for cases was 187.4±5 months, and the 5-year OS was 91.8 and RFS was 83.5.

CONCLUSION

Identifying low-risk patients and reducing treatment intensity will protect patients from long-term side effects. Infection and pulmonary toxicity are among the primary causes of decreased survival in Hodgkin lymphoma.

Keywords: child; Hodgkin lymphoma; relapse.

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INTRODUCTION

Pediatric lymphomas are mainly classified into Hodgkin lymphoma and non-Hodgkin lymphoma. Hodgkin lymphoma accounts for 6% of pediatric cancers and 40% of pediatric lymphomas.[1] These tumors are rare in children under the age of 5 but are more common during adolescence. They occur more frequently in males than in females. Patients are often diagnosed with abnormally enlarged lymph nodes. The most common subtype is nodular sclerosing Hodgkin lymphoma.

Hodgkin lymphoma in childhood is a disease with a survival rate exceeding 95%. Reducing treatment intensity while maintaining survival may decrease long-term side effects.[2] Prognostic factors can assist in distinguishing between low-risk and high-risk patients and in administering reduced-dose treatment to the low-risk group. In our cohort, we aimed to assess our treatment outcomes and the effect of prognostic factors. Poor prognostic factors in Hodgkin lymphoma include anemia, the presence of B symptoms, bulky disease, pericardial/pleural effusion, elevated erythrocyte sedimentation rate (ESR), leukocytosis, hypoalbuminemia, and male sex.[3] With the introduction of positron emission tomography (PET), it has been observed in adults that a favorable treatment response after two cycles is the most significant factor influencing treatment success.[4,5] The use of PET has increased, although pediatric data remain limited.[6] This study aimed to retrospectively examine the treatment outcomes and the effect of prognostic factors on survival in pediatric patients treated for Hodgkin lymphoma.

MATERIALS AND METHODS

The study was approved by the Bursa Uludağ University Ethics Committee (No: 2025/817/15-4, Date: 15/09/2025) and conducted according to the Helsinki Declaration.

The study included 115 pediatric patients treated for Hodgkin lymphoma at our clinic between 2007 and 2024. The patients' demographic data, age at diagnosis, disease stage, presenting symptoms, outcome, complete blood count parameters, and PET results were retrospectively reviewed from their medical records. The presence of accompanying immunological or rheumatological disorders was assessed in the patients' medical histories. The presence of bulky disease was accepted in the presence of a mass >200 ml. The ABVD (adriamycin, bleomycin, vinblastine, and dacarbazine) regimen was administered as the treatment protocol.

Statistical Analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences v. 28.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to determine patients' demographic characteristics. Data were expressed as mean±standard deviation and median (minimum–maximum). Statistical significance was set at $p<0.05$. Normally distributed data were compared using Student's t-test and the chi-square test, while non-normally distributed data were compared using the Mann-Whitney U test.

RESULTS

The mean age at diagnosis for the 115 patients included in the study was 12.3±4 years (Range: 2–18 Years). Of the cases, 45.2% (n=52) were female and 54.8% (n=63) were male. Two patients had previously been treated for acute lymphoblastic leukemia before their Hodgkin lymphoma diagnosis. In addition, one patient was receiving intravenous immunoglobulin therapy due to common variable immunodeficiency, and two patients were receiving colchicine therapy for familial Mediterranean fever.

According to disease stage, 6.1% of cases were stage I, 43.5% (n=50) stage II, 33% (n=38) stage III, and 17.4% (n=20) stage IV. Histopathological results showed that 76.5% (n=88) of patients had the nodular sclerosing type, 15.7% (n=18) the mixed cellularity type, 3.5% (n=4) the lymphocyte-rich type, and 0.9% (n=1) the lymphocyte-depleted type Hodgkin lymphoma, while the subtype could not be determined in four patients.

The mean hemoglobin value of complete blood count parameters was 11.16±1.6 g/dL (Range: 7–16). Of the patients, 18.3% (n=21) had mild anemia, 7% (n=8) had moderate anemia, and 6.1% (n=7) had severe anemia. The patients were divided into two groups based on the presence or absence of anemia, and their demographic data, presence of B symptoms, relapse status, and survival were compared (Table 1).

Anemia was more frequently observed in patients with advanced-stage disease (p=0.04). The frequency of B symptoms was significantly different in patients with anemia (p=0.03). Although relapse was more frequently observed in this group, no statistically significant difference was found compared to the other group. The mean corpuscular volume value was 68.9±6.8 fL in patients with hemoglobin levels below 11 g/dL, and the mean red cell distribution width(RDW) value was 19.7±5.4. Among patients with anemia, 61.1% (n=22) had hypochromic microcytic anemia and 38.9% (n=14) had normochromic normocytic anemia. When

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Table 1 Comparison of patients according to hemoglobin levels

	Hemoglobin level				p
	<11 g/dL (n=36)		≥11 g/dL (n=79)		
	n	%	n	%	
Age (years)	12.3±4.1		12.3±4.07		>0.05
Sex					>0.05
Female	18	50	34	43	
Male	18	50	45	57	
Disease stage					**0.04**
I	2	5.6	5	6.3	
II	9	25	41	51.9	
III	14	38.9	24	30.4	
IV	11	30.6	9	1.4	
Presence of B symptoms	23	63.9	22	27.8	**0.03**
Relapse/refractory disease	8	22.2	11	13.9	>0.05
Outcome					0.05
Mortality	5	13.9	5	6.3	
Survival	31	86.1	74	93.7	

comparing patients with normocytic and microcytic anemia in terms of B symptom frequency, no significant difference was observed (p=0.134).

At the end of treatment, PET results showed PET negativity in 59.1% (n=68) of patients, progressive/refractory disease in 7% (n=8), and partial PET response in 6.1% (n=7). PET results were unavailable for 32 patients. The PET results were compared between patients with and without relapse/refractory disease (Table 2).

During follow-up, relapse/refractory disease was observed in 16.5% (n=19) of patients. Seven patients with relapse/refractory disease underwent autologous stem cell transplantation, and 2 underwent allogeneic stem cell transplantation. Prognostic factors were compared between patients with and without relapse/refractory disease. The mean age of the relapse group was higher (14 vs. 11.9 years). Relapse was more common in patients with advanced-stage disease (p=0.007). Leukocyte counts were higher, hemoglobin levels were lower, and platelet counts were significantly higher in the relapse group compared to the other group. Furthermore, ESR was higher (p=0.039) and the frequency of B symptoms was greater (p=0.001) in the relapse group. However, there was no significant difference between these two groups regarding bulky disease (p=0.166) (Table 2).

Patients received ABVD chemotherapy. Stage I cases were given two cycles, stage II three cycles, stage III four cycles, and stage IV six cycles of ABVD. Following chemotherapy, patients underwent involved-field radiotherapy (IFRT). Radiotherapy total dose for gross residual disease was 30.6 Gy and for microscobic disease was 25Gy. Stage I and stage IIA patients were given only chemotherapy. Stage IIB, III and, IV were given radiotherapy and chemotherapy. The mean follow-up period was 90±52 months (Range: 6–200), and 8.7% (n=10) of patients died during follow-up. Six patients died due to infection, pneumonia, or respiratory failure, and four died due to disease progression. The mean survival time for the cases was 187.4±5 months, and the, 5-year OS was 91.8 and RFS was 83.5 (Fig. 1).

DISCUSSION

Hodgkin lymphoma is the third most common malignancy in childhood in developing countries. The five-year survival rate exceeds 95%. The aim is to reduce treatment intensity to minimize long-term side effects. Research continues to identify which patients may benefit from reduced treatment intensity. In our study, we aimed to evaluate the response to ABVD chemotherapy and to examine prognostic factors. Previous studies have identified male sex as a factor associated with reduced treatment success.[7] In our analysis of patients with relapse/refractory disease, there was no difference in sex distribution compared to the other group. Age was noticeably higher, but the difference was not statistically significant. Another study conducted in Turkey identified anemia, leukocytosis, elevated ESR, and older age as poor prognostic factors. In that study, the mixed cellularity type was more common.[8] In our study, 76.5% of cases were of the nodular sclerosing variant. We considered that the change in variant distribution compared to previous years may be related to improvements in socioeconomic status, living conditions, and the age of exposure to infections.

In a study conducted by the Children's Oncology Group, according to the Childhood Hodgkin International Prognostic Score (CHIPS), which consists of stage IV disease, large mediastinal mass, albumin <3.5, and presence of fever, the group with the highest score had an event-free survival (EFS) of 69%.[9] In our cohort, 73.7% of patients with relapse had stage 3–4 disease, a proportion significantly higher than in the other group. Patients without bulky disease were classified as low-risk by the Children's Oncology Group, while stage IA/IIA patients with bulky disease were consid-

Table 2 Comparison of patients with and without relapse/refractory disease

	Relapse group n=19		Non-relapse group n=96		p
	n	%	n	%	
Age (years)	14±3 (7–18)		11.9±4.1 (2–18)		0.061
Sex					0.479
Female	10	52.6	42	43.7	
Male	9	47.4	54	56.3	
Disease stage					**0.007**
I	1	5.3	6	6.3	
II	4	21.1	46	47.9	
III	6	31.6	32	33.3	
IV	8	42.1	12	12.5	
Bulky disease	2	10.5	9	9.3	0.166
PET result					**0.000**
CR	6	31.6	62	64.6	
PR	2	10.5	5	5.2	
Refractory	8	42.1	0	0	
Not available	3	15.8	29	30.2	
Pathology result					0.156
NS	17	89.4	71	74	
MS	1	5.3	17	17.7	
LZ	1	5.3	3	3	
LD	0	0	1	1	
Undetermined	0	0	4	4.2	
B symptoms					**0.001**
Present	14	73.7	31	32.3	
Absent	5	26.3	65	67.7	
LDH	282.11±86.6		270.78±94.78		0.401
ESR	60.11±38.14 (2–120)		41.14±34.7 (2–120)		**0.039**
Leukocyte count	11892±6623 (2900–27.600)		10284±4878 (3140–39340)		0.326
Neutrophil count	8871±6112 (580–25000)		7100±4682 (1030–35040)		0.243
Lymphocyte count	1774±881 (427–3190)		2122±993 (383–5370)		0.175
Eosinophil count	138±136 (30–538)		223±266 (0–1700)		0.076
Hemoglobin	10.86±1.4 (8–15)		11.2±1.6 (7–16)		0.192
Platelet count	453000±141756		370813±115805		**0.017**

NS: Nodular sclerosing type; MS: Mixed cellularity type; LZ: Lymphocyte-rich type; LD: Lymphocyte-depleted type

ered intermediate risk.[10] Bulky disease and B symptoms are among the factors that reduce survival.[11] In our cohort, bulky disease was not associated with an increased risk of relapse. This may be due to the small number of patients or the relatively large proportion of patients without PET imaging.

Anemia is one of the poor prognostic factors observed in approximately 40% of patients diagnosed with Hodgkin lymphoma.[12] In Hodgkin lymphoma, elevated IL-6 levels caused by inflammation are correlated with anemia.[13] Increased interleukin-6 leads to elevated hepcidin levels, reducing iron absorption and increasing its storage as ferritin. Due to increased inflammation in advanced-stage disease, anemia is more frequently observed in these patients. Patients presenting with anemia have been found to have lower disease-free survival.[14,15] In our study, relapse was more frequent in patients with anemia. Normochromic normocytic anemia, associated with anemia of chronic disease, is more commonly observed in Hodgkin lymphoma.[12] Patients with normochromic normocytic anemia may present more frequently with B symptoms.[16,17] However, in our study, no significant difference was observed between patients with hypochromic microcytic anemia and those with normochromic normocytic anemia in terms of the frequency of B symptoms.

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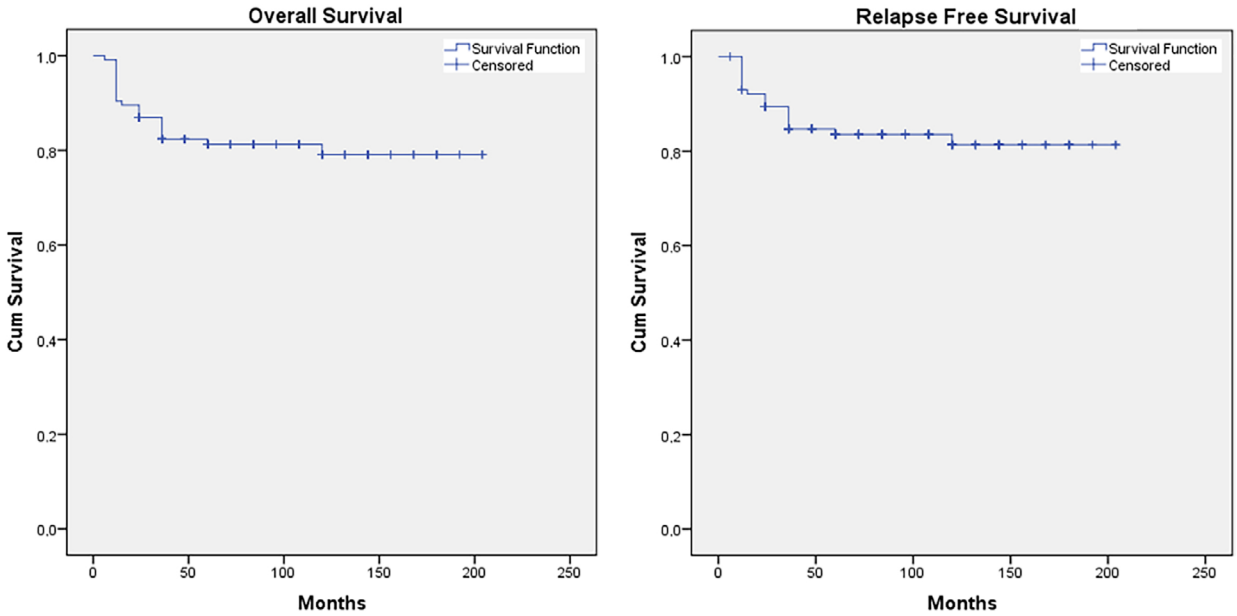

Fig. 1. Kaplan- Meier survival curve (Overall survival-relapse free survival).

Leukocytosis and lymphopenia have been associated with reduced disease-free survival in Hodgkin lymphoma.[14] In our study, the relapse/refractory disease group had higher leukocyte counts, lower lymphocyte counts, and lower eosinophil counts compared to the other group, but these differences were not statistically significant. Platelet counts were significantly higher in the relapse group. Elevated ESR is more frequent in advanced-stage cases. An ESR of <20 mm/h, the presence of the mixed cellularity type, and a PET-negative status after one cycle of chemotherapy have been associated with better EFS.[18] In our study, ESR was significantly higher among patients with relapse.

Between 25% and 40% of patients diagnosed with Hodgkin lymphoma present with B symptoms,[19] which include fever, night sweats, and unintentional weight loss of more than 10% in the last six months. B symptoms have been associated with reduced EFS.[9] In our study, B symptoms were more common in patients with relapse. B symptoms were also more frequently observed in patients with advanced-stage disease, anemia, elevated ESR, and higher platelet and leukocyte counts.

In studies on adults, patients without a favorable PET response after two cycles have been found to have a higher risk of relapse.[4,5] At our clinic, interim PET scanning has only recently been implemented; therefore, such data were unavailable during the study. However, we observed that patients who did not achieve a complete response on PET after chemotherapy had lower disease-free survival. All patients who died due to Hodgkin lymphoma progression in our cohort had been diagnosed before 2013, prior to the introduction of treatments such as the monoclonal antibody brentuximab vedotin or checkpoint inhibitors such as nivolumab. Other deaths were due to treatment-related complications. Ongoing studies aim to reduce treatment intensity while maintaining survival to minimize late treatment-related effects.[20] At our clinic, prophylaxis against infections is not routinely used in patients with Hodgkin lymphoma. Of the patients who died, 60% (n=6) died due to infection, pneumonia, or respiratory failure. One of the most important reasons for this may be pulmonary toxicity caused by bleomycin dosage. In our cohort bleomycin cumulative dosage was 120mg/m2. In a study conducted by Özkan et al.,[21] pulmonary function tests performed on patients diagnosed with Hodgkin lymphoma and receiving bleomycin revealed abnormalities in approximately 40% of patients. Therefore, although pulmonary function tests were not performed in our patients, the cause of their acute lung failure and death may have been related to bleomycin toxicity.

In a multicenter study in adult patients with Hodgkin lymphoma, bleomycin was omitted from the treatment of interim PET-negative patients, and therapy was continued as AVD. Compared with patients who continued ABVD, those receiving AVD had fewer pul-

monary complications, without compromising treatment efficacy.[22] In another pediatric study, similar in sample size and study period, 115 patients were included and received either the EuroNet-PHL-C1 or DAL/GPOH-HD protocol. In that study, relapse/progression was observed in 16 patients, similar to the rate in our study, and only one patient died.[6] We consider that the higher mortality rate in our study compared to that cohort was due to chemotherapy-related toxicity.

In conclusion, Hodgkin lymphoma is a disease with highly favorable outcomes among pediatric malignancies. Research to reduce long-term side effects continues. Based on the prognostic factors identified in our cohort, patients with favorable risk profiles may be suitable candidates for treatment de-escalation strategies, which could help reduce long-term treatment-related toxicity without compromising survival outcomes.

Ethics Committee Approval: The study was approved by the Bursa Uludağ University Ethics Committee (no: 2025/817/15-4, date: 15/09/2025).

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REFERENCES

1. Sherief LM, Elsafy UR, Abdelkhalek ER, Kamal NM, Elbehedy R, Hassan TH, et al. Hodgkin lymphoma in childhood: Clinicopathological features and therapy outcome at 2 centers from a developing country. Medicine 2015;94:e670.
2. Mauz-Körholz C, Metzger ML, Kelly KM, Schwartz CL, Castellanos ME, Dieckmann K, et al. Pediatric Hodgkin lymphoma. J Clin Oncol 2015;33:2975–85.
3. Board PATE. Hodgkin lymphoma treatment (PDQ®): Health professional version. PDQ Adult Treatment Editorial Board. Available at: https://pubmed.ncbi.nlm.nih.gov/26389473/. Accessed Aug 7, 2025.
4. Agostinelli C, Gallamini A, Stracqualursi L, Agati P, Tripodo C, Fuligni F, et al. The combined role of biomarkers and interim PET scan in prediction of treatment outcome in classical Hodgkin's lymphoma: A retrospective, European, multicentre cohort study. Lancet Haematol 2016;3:e467–79.
5. Gallamini A, Rossi A, Patti C, Picardi M, Di Raimondo F, Cantonetti M, et al. Interim PET-adapted chemotherapy in advanced Hodgkin lymphoma (HL). Results of the second interim analysis of the Italian GITIL/FIL DH0607 trial: 118. Hematol Oncol 2015;33:163–4.
6. Yadgarov MY, Dunaykin MM, Shestopalov GI, Kailash C, Kireeva ED, Myakova NV, et al. Prognostic value of baseline and interim [18F]FDG PET metabolic parameters in pediatric Hodgkin's lymphoma. Eur J Nucl Med Mol Imaging 2024;51:1955–64.
7. Rühl U, Albrecht M, Dieckmann K, Lüders H, Marciniak H, Schellenberg D, et al. Response-adapted radiotherapy in the treatment of pediatric Hodgkin's disease: An interim report at 5 years of the German GPOH-HD 95 trial. Int J Radiat Oncol Biol Phys 2001;51:1209–18.
8. Büyükpamukçu M, Varan A, Akyüz C, Atahan L, Özyar E, Kale G, et al. The treatment of childhood Hodgkin lymphoma: Improved survival in a developing country. Acta Oncol 2009;48:44–51.
9. Schwartz CL, Chen L, McCarten K, Wolden S, Constine LS, Hutchison RE, et al. Childhood Hodgkin International Prognostic Score (CHIPS) predicts event-free survival in Hodgkin lymphoma: A report from the Children's Oncology Group. Pediatr Blood Cancer 2017;64:e26278.
10. Lo AC, Dieckmann K, Pelz T, Gallop-Evans E, Engenhart-Cabillic R, Vordermark D, et al. Pediatric classical Hodgkin lymphoma. Pediatr Blood Cancer 2021;68:e28562.
11. Nachman JB, Sposto R, Herzog P, Gilchrist GS, Wolden SL, Thomson J, et al. Randomized comparison of low-dose involved-field radiotherapy and no radiotherapy for children with Hodgkin's disease who achieve a complete response to chemotherapy. J Clin Oncol 2002;20:3765–71.
12. Cuccaro A, Bartolomei F, Cupelli E, Galli E, Giachelia M, Hohaus S. Prognostic factors in Hodgkin lymphoma. Mediterr J Hematol Infect Dis 2014;6:e2014053.
13. Hohaus S, Massini G, Giachelia M, Vannata B, Bozzoli V, Cuccaro A, et al. Anemia in Hodgkin's lymphoma: The role of interleukin-6 and hepcidin. J Clin Oncol 2010;28:2538–43.
14. Smith RS, Chen Q, Hudson MM, Link MP, Kun L, Weinstein H, et al. Prognostic factors for children with Hodgkin's disease treated with combined-modality therapy. J Clin Oncol 2003;21:2026–33.
15. Oguz A, Karadeniz C, Okur FV, Cıtak EC, Pınarlı FG, Bora H, et al. Prognostic factors and treatment outcome in childhood Hodgkin disease. Pediatr Blood Cancer 2005;45:670–5.
16. Barber NA, Bierman PJ. Recognizing unusual manifestations of Hodgkin lymphoma. Curr Hematol Malig Rep 2012;7:186–92.

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doi: 10.5505/tjo.2025.4689

17. Sincan G, Kılıç AF, Sincan S, Erdem F. Prevalence and prognostic significance of anemia in lymphoma. Med J Bakirkoy 2024;20(1):42–7.
18. Keller FG, Castellino SM, Chen L, Pei Q, Voss SD, McCarten KM, et al. Results of the AHOD0431 trial of response adapted therapy and a salvage strategy for limited stage, classical Hodgkin lymphoma: A report from the Children's Oncology Group. Cancer 2018;124:3210–9.
19. Punnett A, Tsang RW, Hodgson DC. Hodgkin lymphoma across the age spectrum: Epidemiology, therapy, and late effects. Semin Radiat Oncol 2010;20:30–44.
20. Kahn JM, Mauz-Korholz C, Hernandez T, Milgrom SA, Castellino SM. Pediatric and adolescent Hodgkin lymphoma: Paving the way for standards of care and shared decision making. Am Soc Clin Oncol Educ Book 2024;44:e432420.
21. Özkan EM, Küpeli S, Özcan D, Özkan A, Sezgin G, Bayram İ. Assessment of respiratory functions in pediatric oncology patients receiving bleomycin treatment. Cukurova Med J 2025;50:83–9.
22. Johnson P, Federico M, Kirkwood A, Fosså A, Berkahn L, Carella A, et al. Adapted treatment guided by interim PET-CT scan in advanced Hodgkin's lymphoma. N Engl J Med 2016;374:2419–29.