Original Article *Iran J Ped Hematol Oncol. 2020, Vol 10, No 4, 203-208*

Evaluation of clinicopathologic and Survival Characteristic of Childhood and Adolescent Hodgkin's lymphoma

Fariba Binesh MD[1,2*], Azam Sadat Hashemi MD[2], Nazila Naghibzadeh MD[3], Fatemeh Pourhosseini MSc[1], Sara Mirhosseini MD[4]

1. Department of Pathology, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
2. Hematology and Oncology Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
3. Department of Pediatric, Shahid Sadoughi University of Medical Sciences, Yazd, Iran
4. Shahid Sadoughi University of Medical Sciences, Yazd, Iran

*Corresponding author: Dr Fariba Binesh, Department of Pathology, Shahid Sadoughi University of Medical Sciences, Yazd, Iran. Email: binesh44@yahoo.com. ORCID ID: 0000-0002-4260-6137

Received: 02 June 2020 **Accepted:** 28 August 2020

Abstract

Background: Given that Hodgkin's lymphoma (HL) accounts for 5%–6% of pediatric malignancies, we investigated the clinical characteristics and survival of pediatric patients with HL in our center.

Materials and methods: In this cross sectional and retrospective study, the medical charts of all patients under the age of 18 diagnosed with HL from 2006 to 2016 at Shahid Sadoughi Hospital Yazd, Iran, were retrieved. Data were analyzed by SPSS (version 18) using K square and T-Test. Survival was analyzed using Kaplan-Meier estimates, and multivariate analysis was performed using the Cox regression method.

Results: This study included 34 patients. In terms of gender, there were 20 boys and 14 girls in this study. The mean age of the patients was 10.42 years. The most common subtype of HL was mixed cellularity. Regarding disease stage, 55.9% of the patients were in stage I. All subtypes except for nodular sclerosis were more common in boys. The mean survival of patients in this study was 151.68 months. At the end of the study, there was just one death. The 5-year survival of patients was 100% and the 10-year survival was 94%. There was no significant relationship between survival and sex, histologic subtype, or the stage of the disease.

Conclusion: The results of the current study showed that majority of our patients had been diagnosed in a low stage and we achieved the best results for 5- and 10- year- overall survival through applied treatment.

Key words: Hodgkin lymphoma, Pediatric, Survival

Introduction

Acute leukemia comprises a heterogeneous Malignant lymphoma is among the most frequent neoplasm seen in pediatric patients. It is a malignant disease of the lymphoreticular system with different clinical manifestations. Malignant lymphomas are divided into two major groups, namely Hodgkin's lymphoma (HL) and non HL. HL represents approximately 4% of childhood neoplasms and 15% of adolescent malignant tumors (1). Regarding histology, HL has two main types, including classical and nodular lymphocyte predominant types. The former is further divided into four subtypes. The Reed-Sternberg cell, a hallmark microscopic feature in classic types (nodular sclerosing, lymphocyte-rich, lymphocyte-depleted, and mixed cellular), but it is not seen or only rarely seen in nodular lymphocyte predominant HL. The etiology of HL is obscure. The correlation between HL and Epstein-Barr (EB) virus varies. This association in immunocommponent patients is reported 30-40%, while this figure in immunocompromised ones reaches to 80% (2). There are epidemiological, clinical, and pathological differences of HL based on the geographical location (3). HL in developing countries occurs at a younger age. Moreover, the disease in these societies is usually presented in advanced stages. In addition, the prognostic factors are different in poor and rich nations. Despite all this, the treatment of HL has achieved high cure rates in the world (4). Nowadays, HL is a curable tumor. Through combined chemoradiation

[DOI: 10.18502/ijpho.v10i4.4403]

therapy, cure rate is about 80-90%. Combined chemoradiation therapy was shown to result in superior disease control compared with radiation therapy alone (5). The lack of information about pediatric HL in Yazd province has led us to do this research. We analyzed the sociodemographic profile, the characteristics of the disease, and the survival in pediatric patients with HL treated at Shahid Sadoughi hospital.

Materials and Methods

In this cross sectional and retrospective study, the medical records of patients admitted at Shahid Sadoughi Hospital Yazd, Iran, from 2006 to 2016 were reviewed. Sampling was done by taking a census. The medical charts of all patients under the age of 18 diagnosed with HL were retrieved. As study variables, we recorded the patients' hospital registration number; date of admission, and demographic characteristics, including age, gender, sub type of tumor, clinical symptoms, stage, and survival. The data were obtained via the patients' medical records and through phone. Overall survival was calculated from date of diagnosis until death or date of the last follow-up. The patients were staged according to the Ann Arbor Staging system. This study was approved by the Ethics Committee of Shahid Sadoughi University of Medical Sciences, Yazd, Iran (IR.SSU.MEDICINE.REC.1398.003).

Statistical analysis

Data were analyzed by SPSS (version 18) using K square and T-Test. Survival was analyzed using Kaplan-Meier estimates, and multivariate analysis was performed using the Cox regression method. Patients with incomplete information were excluded from the study. P-value < 0.05 was considered statistically significant. This work was conducted in accordance with the Declaration of Helsinki (2000).

Results

This study included 34 patients. In terms of gender, there were 20 (58.8%) boys and 14 (41.2%) girls in this study. The mean age of the patients was 10.42 years with a standard deviation of 4.75 and range of 3 to 18 years. Among the patients, 1case (2.9%) died during the study, 28 patients (82.4%) were alive, and no data were available about 5 cases. The most common subtype of HL was mixed cellularity with 55.9% frequency and then was nodular sclerosis with 32.4% (Table I). Regarding stage of the disease, 55.9% of patients were in stage I, 23.5% in Stage II, 2.9% in stage III, and 17.6% in stage IV (Table II). The most common clinical signs were lymphadenopathy (41.2%) and then constellation of fever with sweats and lymphadenopathy (26.5%) (Table III). Mixed cellularity type was 63.2% in boys and 36.8% in girls. Nodular Sclerosis was more common in girls with a frequency of 54.5%. However, other subtypes were more common in boys. There was no significant relationship between different subtypes of HL and gender of the patients ($p = 0.65$) (Table- IV). No significant correlation was observed between the various subtypes of HL and the stage of the disease ($p=0.96$). The results of the study showed that the mean survival of the patients in this study was 151.68 months with a standard error of 0.34 (Figure-1). At the end of study, 28 cases out of 29 cases (96.6%) were alive. Our results showed that the 5-year survival of patients was 100% and the 10-year survival was 94%. Owing to the death of just one boy, it was not possible to assess the mean survival time. According to $p = 0.46$, there was no significant relationship between survival and sex of the patients (Figure-2). The 5-year survival of boys and girls was 100%. However, the 10-year survival rate for boys was about 90 percent and for girls about 100 percent. There was no significant relationship between survival and the subtype of HL ($p = 0.56$) (Figure-3). No significant relationship was found between survival and disease stage ($p = 0.198$) (Figure4).

[DOI: 10.18502/ijpho.v10i4.4403]

Table I:Frequency distribution of various subtypes of Hodgkin's lymphoma in patients

Subtype	Number	Percent
Mixed cellularity	19	55.9%
Nodular sclerosis	11	32.4%
Unclassified	1	2.9%
Lymphocyte rich	2	5.9%
Lymphocyte predominant	1	2.9%
Sum	34	100%

Table II: Frequency distribution of disease stage in patients

tim	number	percent
I	19	**55.9%**
II	8	**23.5%**
III	1	**2.9%**
IV	6	**17.6%**
Sum	34	**100**

Table III: Frequency distribution of clinical symptoms in patients

Sign	Number	Percent
Fever+sweating+lymphadenopathy	9	26.5
Submandibular mass	1	2.9
Fever+ lymphadenopathy	1	2.9
Cervical mass	2	5.9
lymphadenopathy Cervical	14	41.2
Dyspnea	4	11.8
Inguinal lymphadenopathy	1	2.9
Cervical and axillary lymphadenopathies	2	5.9
Sum	34	100

Table IV: Frequency of pathologic subtypes according to sex

subtype sex	boy		girl		sum	
	number	percent	number	percent	number	percent
Mixed cellularity	12	63.2	7	36.8	19	100
Nodular sclerosis	5	45.5	6	54.5	11	100
Unclassified	1	100	0	0	1	100
Lymphocyte rich	1	50	1	50	2	100
Lymphocyte predominant	1	100	0	0	1	100
Sum	20	58.8	14	41.2	41.24	100
P value	0.65					

[DOI: 10.18502/ijpho.v10i4.4403]

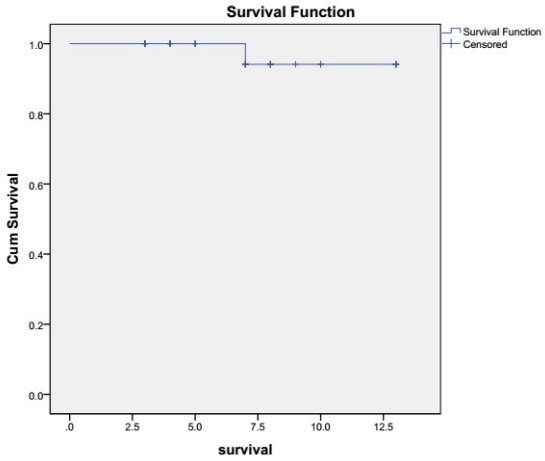

Figure-1. Overall Survival in children and adolescents with Hodgkin lymphoma

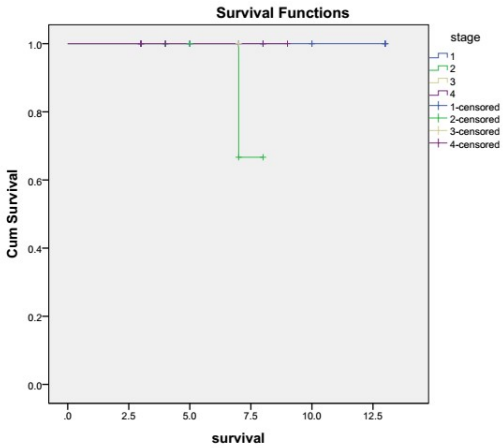

Figure 4. Overall Survival and disease stage in children and adolescents with Hodgkin lymphoma

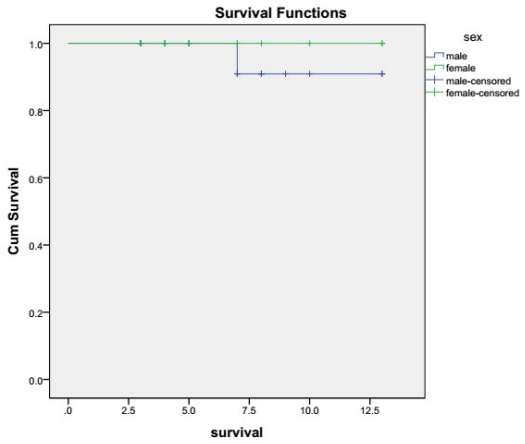

Figure 2. Overall Survival and sex in children and adolescents with Hodgkin lymphoma

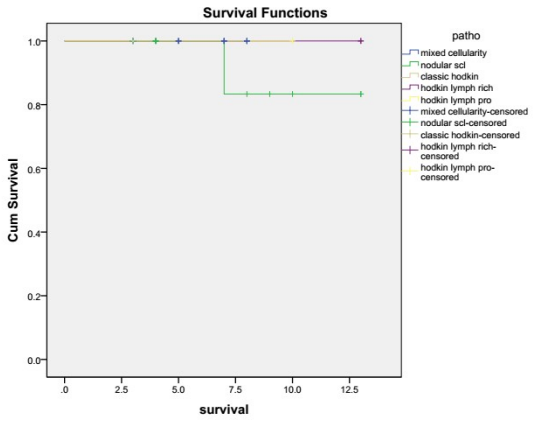

Figure 3. Overall Survival and histologic subtypes in children and adolescents with Hodgkin lymphoma

Discussion

HL is a malignant disease of the lymphoreticular system with different clinical manifestations. Nowadays, more than 90% of pediatric patients with HL will survive 5 or more years (6). There is a dearth of epidemiological studies conducted on the pediatric HL in our region and this factor induced us to carry out this study to describe the clinical and its epidemiological characteristics, assess it survival, and search for its possible prognostic associations with the variables under analysis. In this study, the mean age of the patients was 10.42 years with a standard deviation of 4.75 and range of 3 to 18 years. It was lower than that showed by a study done in a Western country (median age: 15.6) (6) , but similar to the results of other developing countries. For example in one cohort, the mean age of patients was 9.0 years (7). Other studies from the developing nations also confirmed younger age for HD presentation (8). A research from Egypt reported median age of 6 years (9). This younger median age at the time of diagnosis in the present study and studies from other developing countries may be related to the high incidence of EB virus infection at an early age in our locations; however, this conclusion should be

[DOI: 10.18502/ijpho.v10i4.4403]

authenticated by assessing the EB virus genomes in the tumor cells (8). In our study, a vast majority of the patients were presented with cervical lymph nodes enlargement at first. It is in consistent with other studies (10). For example, Ashraf and Göknar showed that more than 70 percent of their patients presented with the early stage disease had cervical or supraclavicular nodes involvement (7,11). Our results revealed that the disease was higher in males than females. Male to female ratio, on the other hand, in one study was >4:1(7), which was higher than what was shown in developed countries (12). However, the male to female ratio in another study was 1.7:1(9), which was similar to us but different from another study (13). In that work (13), there was a male preponderance which was similar to other Indian reports (14, 15). The reason for this difference may be due to obstacles in some cultures in relation to females visiting medical centers compared with males (16). However, we believe that in addition to this matter, the disease is more common in males. This male preference is also shown in another study (13). Histologically, in the present study mixed cellularity was the most common histologic subtype. It was shown that the most common histologic subtype in the Western countries is nodular sclerosis (17), but in Ashraf's study, mixed cellularity was the most frequently diagnosed subtype (7). Other studies from developing nations reported a similar histopathologic distribution (8, 18, 19). This may be due to the etiological link between the disease and the EBV infection (20). Most of our patients were in stage I. On the contrary, stage II was the most common stage in one study (10). Previous works reported advanced disease in their patients (7, 18, 21). In the present study, the overall survival was 151.68 months. Ashraf et al., presented a five-year survival and event free survival of 89.6% and 82.1%, respectively (7). Other studies also revealed an overall survival ranging from 79% to 92.7% and event free survival ranging from 53% to 87.9% (13). To explain some differences among various studies, we should say that in addition to the variation in the characteristics of the disease, there are differences in the applied treatment modalities and the response to them. Racial factor is effective in the exposure of the underlying risk factors and in the access to high-quality and timely diagnosis. In developing countries, the limited availability of resources and optimal follow-up are also important factors. In this regard the results of one study showed that black patients with HL were younger at the time of diagnosis and had higher stages and unfavorable histologic subtypes. As a result, they had a worse outcome (22) .We did not find any significant relationship between overall survival and sex, histologic subtype, or disease stage. The optimal treatment regimen in children remains controversial. The main limitation of our study was was its short follow-up. In addition, our sample size was small.

Conclusion

The current study showed that the patients with HL in our center referred in low stage of the disease. In addition, it was found that the histology subtype did not have any effect on the overall survival. Although Iran is a developing country, we achieved a very good overall survival in our patients with HL.

Conflict of interest

The authors declare no conflict of interest.

References

1. Ward E, Desantis C, Robbins A, Kohler B, Jemal A. Childhood and adolescent cancer statistics. CA Cancer J Clin 2014; 64(2): 83–103.

2. Carbone A, Spina M, Gloghini A, Tirelli U. Classical Hodgkin's lymphoma arising in different host's conditions: pathobiology parameters, therapeutic

[DOI: 10.18502/ijpho.v10i4.4403]

options, and outcome. Am J Hematol 2011; 86(2):170–179.
3. Sheikhpour R, Aghaseram M. Diagnosis of acute myeloid and lymphoblastic leukemia using gene selection of microarray data and data mining algorithm. Sci J Iran Blood Transfus Organ 2016; 12 (4): 347-357.
4. Jain S, Kapoor G, Bajpai R. ABVD based therapy for Hodgkin lymphoma in children and adolescents: Lessons learnt in a tertiary care oncology center in a developing country. Pediatr Blood Cancer 2016; 63:1024-1030.
5. Fermé C, Eghbali H, Meerwaldt J.H. Chemotherapy plus involved-field radiation in early-stage Hodgkin's disease. N Engl J Med 2007; 357: 1916-1927.
6. Best T, Li D, Andrew D Skol AD. Variants at 6q21 implicate PRDM1 in the etiology of therapy-induced second malignancies after Hodgkin's lymphoma Nat Med 2011; 17(8): 941-943.
7. Ashraf Muhammad S. Fozia N, Mohammad Y. Characteristics and survival outcomesof children with hodgkin lymphoma treated primarily with chemotherapy
J Pediatric Hematol Oncol 2019; 41 (6): 452-456.
8.Arya LS, Dinand V, Thavaraj V. Hodgkin's disease in Indian children: outcome with chemotherapy alone. Pediatr Blood Cancer 2006; 46:26–34.
9.Sherief LM, Elsafy UR, Abdelkhalek ER, Kamal NM, Elbehedy R, Hassan TH. Hodgkin lymphoma in childhood: Clinicopathological features and therapy outcome at 2 centers from a developing country. Medicine (Baltimore) 2015; 94: e670-e680.
10. Abdallah BK, Rashid NG, Tawfiq SA. Pediatric hodgkin lymphoma in Iraq-KRG-Sulaimani. Iraqi JMS 2019; 17(1): 12-17.
11. Göknar N, Çakir E, Çakir FB. A difficult dase of hodgkin lymphoma with differential diagnosis of tuberculosis and sarcoidosis. Hematol Rep 2015; 7:5644-5665.
12. Graciela Abriata K, Forman D, Sierra M, Cancer Epidemiol 2016; 44S: S158–S167.
13. Gupta V, Singh TB, Gupta SK. Response and relapses in pediatric Hodgkin's lymphoma treated with chemotherapy alone. Indian J Med Paediatr Oncol 2019; 40: 341-346.
14. Jain S, Kapoor G, Bajpai R. ABVD-based therapy for Hodgkin lymphoma in children and adolescents: Lessons learnt in a tertiary care oncology center in a developing country. Pediatr Blood Cancer 2016; 63: 1024-1030.
15. Verma N, Kumar A. Treating Hodgkin's lymphoma in a resource poor setting: Challenges and outcome. Cancer Oncol Res 2015; 3:311-316.
16. Maddi RN, Linga VG, Iyer KK, Chowdary JS, Gundeti S, Digumarti R. Clinical profile and outcome of adult Hodgkin lymphoma: Experience from a tertiary care institution. Indian J Med Paediatr Oncol 2015; 36: 255-260.
17. Horner MJ, Ries LAG, Krapcho M, Neyman N, Aminou R, Howlader N. SEER CS; 75:2006-2009.
18. Trehan A, Singla S, Marwaha RK, Bansal D, Srinivasan R. Hodgkin lymphoma in children: Experience in a tertiary care centre in India. J Pediatr Hematol Oncol 2013; 35:174-179.
19. Chandra J, Naithani R, Singh V, Saxena YK, Sharma M, Pemde H. Developing anticancer chemotherapy services in a developing country: Hodgkin lymphoma experience. Pediatr Blood Cancer 2008; 51:485-489.
20. Vockerodt M, Zumla Cader F, Shannon-Lowe C, Murray P. Epstein-Barr virus and the origin of hodgkin lymphoma. Chin J Cancer 2014; 33(12): 591–597.
21.Sindh U. Retrospective analysis of baseline prognostic factors on the outcome of pediatric hodgkin lymphoma in a Tertiary cancer centre. Klin Padiatr 2020; 232(02): 93-99.
22.Khullar K, Rivera-Núñez, Z. Pediatric hodgkin lymphoma: disparities in survival by race. Hema Sphere 2019; S1:188-192.

[DOI: 10.18502/ijpho.v10i4.4403]