original reports abstract

Clinical Characteristics and Histopathological Patterns of Hodgkin Lymphoma and Treatment Outcomes at a Tertiary Cancer Center in Ethiopia

Makka Adam, BSc, MSc[1,2,3,4]; Yonas Bekueretsion, MD[5]; Abdulaziz Abubeker, MD[6]; Fisihatsion Tadesse, MD[6]; Anna Kwiecinska, MD, PhD[7]; Rawleigh Howe, MD, PhD[2]; Beyene Petros, BSc, MSc, PhD[1]; Mats Jerkeman, MD, PhD[3]; and Amha Gebremedhin, MD[6]

PURPOSE In developing countries, Hodgkin lymphoma (HL) affects the young population. In Ethiopia, nearly 70% of the population are < 35 years of age. Therefore, this study aimed to elucidate the age distribution, histopathologic patterns, clinical characteristics and treatment outcomes of HL in Ethiopia.

MATERIALS AND METHODS Data from clinical records of 133 consecutive patients with HL between 2014 and 2019 were reviewed and collected. Formalin-fixed paraffin-embedded tissue blocks of HL cases were collected and used for subtype classification.

RESULTS A total of 68.4% (91) of the patients were male; male-to-female ratio was 2.2:1. The median age was 22 years. The age distribution was 57.1% (76), 30.8% (41), and 2.3% (3) for the age groups (10-29), (30-59), and (60-69) years, respectively. Thirteen percent (12) were associated with HIV. The majority of the cases, 50.4% (67), were of the mixed-cellularity (MCCHL) subtypes and 30% (40) nodular-sclerosis (NSCCHL). Most HIV-associated cases (60%, 6) were of the MCHL subtype. The 4-year overall survival (OS) was 83.1%. The 4-year OS of early-stage patients was 100% and advanced-stage patients with low-risk (International Prognostic Score [IPS] ≤ 2) and high-risk (IPS ≥ 3) were 94.1% and 62.9%, respectively. All patients who received combined-therapy survived, whereas those who received doxorubicin, bleomycin, vinblastine, and dacarbazine only showed a 4-year OS rate of 77.9%.

CONCLUSION HL affects the youngest and most productive population in Ethiopia. The treatment outcome is favorable in both HIV-associated and non–HIV-associated HL. However, the study population was likely a highly selected group as the majority of the Ethiopian population do not have access to specialized care.

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INTRODUCTION

Hodgkin lymphoma (HL) is a distinctive lymphoid neoplasm with a characteristic clinical presentation, epidemiology, and histopathologic pattern.[1] HL was the first lymphoid malignancy to be described, in 1832.[2] HL affects all age groups, but is reported to be most common in age groups between 20 and 34 years.[3] In high-income countries, the onset of HL shows a bimodal distribution. The first peak is observed in the age groups between 15 and 35 years, and a second incidence peak can be observed after the age of 50 years.[4] In low-income countries, HL is among the most common cancers in adolescents and younger adults,[5] and the second peak does not occur.[6,7] In Ethiopia, 70% of the population are younger than 35 years of age.[8,9]

The global incidence of HL is about 3/100,000 per year.[10] The 5-year prevalence for HL in the world, Africa, and Ethiopia is estimated to be (3.6)/100,000, (2.0)/100,000, and (1.5)/100,000, respectively. The estimated mortality rate is (0.30), (0.48), and (0.40) for the world, Africa, and Ethiopia, respectively.[11] Studies conducted to assess the pattern of cancer in Ethiopia have shown a considerable number of patients diagnosed with HL.[7] Recent estimates indicated that hematologic malignancies comprise the third leading cause of cancer and cancer-related mortality in Ethiopia, of which nearly 20% are HL.[7,12]

HL has a unique histomorphologic presentation with a minority of neoplastic cells, which comprise < 1% of the total cell population, and a large majority of non-malignant reactive immune cells.[13] HL has been divided into two major types: classical HL,[14] which accounts for 90% of all cases, and nodular lymphocyte-predominant HL (NLPHL) depending on morphologic, phenotypic, genotypic, and clinical findings.[15] The classical Hodgkin lymphoma (CHL) is further subtyped into nodular sclerosis CHL (NSCHL), lymphocyte-rich CHL (LRCHL), mixed-cellularity CHL (MCCHL), and lymphocyte-depleted CHL (LDCHL)

ASSOCIATED CONTENT

Appendix

Author affiliations and support information (if applicable) appear at the end of this article.

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CONTEXT

Key Objective

Hodgkin lymphoma (HL) has a bimodal distribution in developed countries, the first and second peaks were observed in the age groups 15-34 years and after the age of 50 years, respectively. In developing countries, HL mainly occurs among adolescents and younger adults, and shows a different distribution of histologic subtypes. This study aimed to explore the disease distribution pattern and survival outcomes in an Ethiopian setting.

Knowledge Generated

In Ethiopia, patients' age distribution and histopathologic patterns of HL are different from that in developed countries, with a younger age distribution and a higher incidence of the mixed cellularity subtype. We have confirmed the favorable outcome of current treatment.

Relevance

The treatment outcome of patients with HL is favorable with the standard treatment regimen in a low- or middle-income setting, if augmented with proper diagnosis.

subtypes.[16] In high- and middle-income countries, the predominant subtype is NSCHL,[17,18] whereas in low-income countries, MCCHL and LDCHL subtypes are predominant.[6,19] The incidence of HL has increased in sub-Saharan Africa during the burden of HIV.[20] Probably, HIV increases the risk of HL because of loss of immunity.[21] The majority of HL cases associated with HIV are of MCCHL and LDCHL subtypes.[22]

Ethiopia is one of the sub-Saharan African countries in which cancer is becoming one of the major public health problems. Tikur Anbessa Specialized Hospital (TASH) is the only cancer treatment center in the country. All cancer patients seeking diagnosis and treatment are referred to this hospital. Unfortunately, not all patients can afford the cost of traveling and treatment. In addition, the absence of a cancer registry throughout the country except for the recently launched one by the Addis Ababa city administration contributes to the low estimation of cancer incidence and mortality rate in the country. Thus, it is very difficult to estimate the real picture of incidence and mortality rate of HL. This study is designated to elucidate age distribution, clinical characteristics, histopathologic subtypes, and survival outcome of HL in an Ethiopian setting.

TABLE 1. Primary Antibody Characteristics

Antigen	Clone	Dilution	Supplier	Antigen-Retrieval Method
CD30	Ber-H2	1:50	Agilent/DAKO	PT-Link pH9
CD15	Carb-3	1:50	Agilent/DAKO	PT-Link pH9
PAX5	SP34	1:200	Cell Marque	PT-Link
CD20cy	L26	1:500	Agilent/DAKO	PT-Link pH9
CD3	A0452	1:200	Agilent/DAKO	PT-Link pH9
CD79a	JCB117	1:500	Agilent/DAKO	PT-Link pH9
CD45	2B11 + PD7/26	1:300	Agilent/DAKO	PT-Link pH9
CD57	TB01	1:100	Agilent/DAKO	PT-Link pH9
OCT-2	EPR16570	1:1,000	Abcam	PT-Link pH9
PD-1	NAT105	1:100	Cell Marque	2100 Retriever pH6

MATERIALS AND METHODS

This is a retrospective study of HL cases diagnosed at TASH during the period 2014-2019. The clinical records of 133 HL cases were reviewed, from which demographic data, histopathologic subtypes of HL, stage of the disease, and other related clinical data were collected. At TASH, staging of patients with HL includes detailed history with special attention to the presence or absence and duration of systemic (B) symptoms and pruritus; adequate surgical biopsy; physical examination with particular emphasis to lymph node regions and organs; complete blood count and differential erythrocyte sedimentation rate; plain chest x-rays with measurement of mediastinal mass; abdominal ultrasonographic studies; computed tomography scan of the neck, chest, abdomen, and pelvis; and bone marrow aspiration and biopsy for stage IV disease, and stage III if the patient has cytopenias.

Since there is no electronic cancer or death registry system, patients whose records lacked follow-up data were contacted through their cellphone numbers that were available on the clinical records. Accordingly, 71 of 133 HL cases were included for the overall survival (OS) analysis.

Formalin-fixed paraffin-embedded tissue blocks of the HL cases were collected from the archives of the pathology department of TASH. The tissue blocks were used for classification of HL into CHL and NLPHL subtypes. Cases were reviewed by a specialist in hematopathology (A.K.) and reassessed according to 2016 WHO classification of Tumors of Hematopoietic and Lymphoid Tissues.[16] Two whole sections with 3-4-μm thickness were prepared from each tissue block and stained with hematoxylin and eosin and CD30. A tissue microarray (TMA) was constructed from the collected formalin-fixed paraffin-embedded tissue blocks, a method validated also in HL.[23-25]

TABLE 2. Clinical Characteristics of Patients With HL Diagnosed Within the Study Period

Characteristic of Patients	No.	%
Sex		
Male	91	68.4
Female	42	31.6
Age, years		
0-9	13	9.8
10-19	43	32.3
20-29	33	24.8
30-39	19	14.3
40-49	10	7.5
50-59	12	9
60-69	3	2.3
Stage of the disease		
Stage I	31	26.5
Stage II	46	39.3
Stage III	25	21.4
Stage IV	15	12.8
B-symptoms		
Yes	73	54.9
No	60	45.1
HIV status		
Positive	12	13
Negative	80	87
Total	92	100
HL subtypes		
MCCHL	67	50.4
NSCHL	40	30.1
LDCHL	6	4.5
LRCHL	7	5.3
NLPHL	13	9.8
Total	133	100
WBC count at diagnosis		
Normal (3.98-10.04 × 10^3/μL)	93	70.5
High (> 10.04 × 10^3/μL)	22	16.7
Low (< 3.98 × 10^3/μL)	17	12.9
WBC ≤ 15 × 10^3/μL	114	86.4
WBC > 15 × 10^3/μL	18	13.6
Lymphocyte count at diagnosis (reference interval: 1.18-3.75 × 10^3/μL)		
≥ 1.18 × 10^3/μL	50	38.2
< 1.18 × 10^3/μL	81	61.8
> 0.6 × 10^3/μL	79	59.4
≤ 0.6 × 10^3/μL	52	39.1
Monocyte count at diagnosis (reference interval: 0.24-0.82 × 10^3/μL)		

(Continued on following page)

Slides with TMA sections were stained with the following antibodies (Abs): CD30, CD15, PAX5, CD20, CD79a, CD45, OCT-2, PD-1 and CD57, and CD3 to characterize and subclassify HL. PD-1 and CD57 markers were used for the differential diagnosis of NLPHL, CHL, and T-cell histocyte-rich large B-cell lymphoma.[26] The whole and TMA sections were dewaxed, deparaffinized, and antigen-retrieved either in high pH or in low pH.[27] Polymer-based immunohistochemistry techniques were used to stain the TMA and tissue sections with the Abs.[28] Details of the primary antibodies and dilutions are shown in Table 1.

Descriptive statistics were used to explore the demographic characteristics, clinical variables of HL cases, and treatment modalities. Chi-square test or Fisher's exact test was used to show the differences and distributions of different variables. OS of HL cases in the study was calculated by using the date of diagnosis and time of last date of the patients known to be alive, date of death, or last date of follow-up, and estimated according to the Kaplan-Meier method. Mann-Whitney *U* and Kruskal-Wallis tests were used to analyze the distribution of age among nominal and categorical variables, respectively. Analysis of variance or univariate analysis was used to show the mean differences of age among the groups of categorical variables. A result with *P* value < .05 was considered statistically significant. Ethical clearance was obtained from Addis Ababa University College of Natural Sciences, College of Health Sciences Institutional Ethics review boards, and Ethical Review board of Armauer Hansen Research Institute in accordance with the Declaration of Helsinki.

RESULTS

Out of a total of 133 patients with HL, 68.4% (91) were males and 31.6% (42) females, with a male-to-female ratio of 2.2:1 and a *P* value of < .001 (Table 2). The patients' age ranged between 4 and 66 years, with a median age of 22 years. The most affected age groups in this study were adolescent (10-19 years) and young adults (20-29 years) that accounted for 33.1% (43) and 24.6% (32) of the total number, respectively. The elderly (≥ 60 years) represented only 2.3% (3) of the cases (Appendix Fig A1). There was no significant difference in age distribution between male and female patients. The majority of patients were from Oromia Regional State 35.2% (43), followed by Addis Ababa 27.9% (34) and Amhara Regional State 22.1% (27), as depicted in Appendix Table A1.

Most of the patients 54.9% (73) presented with one or more of the B-symptoms at diagnosis. According to the Ann Arbor staging system,[29] 26.5% (31), 39.3% (46), 21.4% (25), and 12.8% (15) of the patients, respectively, presented with stage I, II, III, and IV at diagnosis. 65.1% (84) of the patients presented with anemia. Hemoglobin levels of < 13.7 g/dL for males and < 11.2 g/dL for females were used to diagnose anemia; 61.8% (81) of the patients presented with lymphocytopenia (*cutoff* < 1.18 × 10^3/μL)

TABLE 2. Clinical Characteristics of Patients With HL Diagnosed Within the Study Period (Continued)

Characteristic of Patients	No.	%
≥ 0.24	60	45.8
< 0.24	71	54.2
Hemoglobin at diagnosis, g/dL (reference interval: male 13.7-17.5 g/dL, female 11.2-15.7 g/dL)		
≥ 13.7 male, ≥ 11.2 female	45	34.9
< 13.7 male, < 11.2 female	84	65.1
> 10.5	70	54
≤ 10.5	59	46
Therapeutic modalities		
ABVD	109	82.0
ABVD and COPDAC	9	6.8
ABVD, COPDAC, and radiotherapy	5	3.8
ABVD and radiotherapy	1	0.8
Missing	9	6.8
Total	133	100
ABVD treatment cycles		
< 4 cycles	3	2.3
4 cycles	42	31.5
6 cycles	55	41.4
8 cycles	17	12.8
Total	117	88.0
Missing	16	12.0
Total	133	100.0
COPDAC treatment cycles		
2 cycles	11	8.3
4 cycles	2	1.5
6 cycles	1	0.8
None	119	89.5
Total	133	100.0

Abbreviations: ABVD, adriamycin (doxorubicin), bleomycin, vinblastine and dacarbazine; CHL, classical Hodgkin lymphoma; COPDAC, cyclophosphamide, vincristine sulfate, prednisone, and dacarbazine; HL, Hodgkin lymphoma; LDCHL, lymphocyte-depleted CHL; LRCHL, lymphocyte-rich CHL; MCCHL, mixed-cellularity CHL; NLPHL, nodular lymphocyte-predominant HL; NSCHL, nodular sclerosis CHL.

and 54.2% (71) with monocytopenia (*cutoff* < $0.24 \times 10^3/\mu L$). MCCHL was the dominant histopathologic subtype 50.4% (67) followed by NSCHL 30.1% (40), as displayed in Table 2. The MCCHL subtype was more common in males 72.1% (44) than in females 27.9% (17), with a ratio of 2.6:1. The distribution of NSCHL subtype among sexes was almost similar, with a ratio of 1.2:1 as depicted in Appendix Table A2. The median age of HL cases was different between the CHL subtype and the NLPHL, 21 and 38 years, respectively, ($P = .004$). MCCHL and NSCHL were more common among patients up to 29 years of age, whereas NLPHL was more common among patients older than 30 years of age (Appendix Fig A2).

HIV results were available for 92 patients, and 13% (12) were positive. 63.7% (7) of these presented with stage I-II at diagnosis. However, 75% (9) of HIV-positive cases were categorized into the group of advanced stage when restaged using B-symptoms. The distribution of HIV-associated HL was similar between males and females in this study. 83.3% (10) of HIV-associated HL cases were within the age group of > 14 years. 60% (6) of HIV-associated HL cases were of the MCCHL subtype followed by NSCHL subtype (3, 30%), as demonstrated in Table 3. Monocytopenia was strongly associated with HIV, 75% (9) of HIV-associated HL had low monocyte counts.

The majority of patients 93.4% (124) were treated with the standard chemotherapy regimen doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD), whereas 6.8% (9) of the patients, all belonging to the pediatric population, were treated with ABVD followed by cyclophosphamide, vincristine sulfate, prednisone, and dacarbazine (COPDAC). 3.8% (5) of the patients received ABVD and COPDAC followed by radiotherapy, and only 0.8% (1) was treated with ABVD followed by radiotherapy. The number of ABVD treatment cycles in this study ranged between 4 and 8 cycles. Three patients (2.3%) received < 4 cycles of ABVD; these patients stopped treatment and follow-up earlier than planned. The number of COPDAC cycles ranged between 2 and 6 cycles. 48.3% (14) of patients with HL within the age group ≤ 14 years were treated with the ABVD regimen only, whereas 51.7% (15) of this age group were treated with combined chemotherapy and of these patients, five had additional radiotherapy. All HL cases within the age group > 14 years were treated with ABVD. A total of 94.7% (36) patient cases with early stage disease received ABVD only, one received combined chemotherapy, and one received combined chemotherapy with radiotherapy. 85.1% (74) and 14.9% (13) of HL cases with advanced-stage disease received ABVD only or combined chemotherapy with or without radiotherapy respectively.

The comparison between patients with complete (71/53.4%) and incomplete follow-up data (62/46.6%) revealed that the distribution of age between these two groups was significantly different ($P = .001$), with median ages of 17 and 25 years, respectively. No significant differences were found in the distribution of sex, stage, WBC and lymphocyte count, IPS (International Prognostic Score), or HL subtype. However, the group with complete survival data presented with lower hemoglobin, higher monocyte count, and was less frequently associated with HIV.

The 4-year OS for patients in this study was 83.1% (Fig 1), with a 19-month median follow-up time. The 4-year OS of patients with early-stage and advanced-stage disease was 100% and 78.2%, respectively. Patients presenting with stage I, II, III, and IV had 4-year OS rates of 94.1%, 76.3%,

TABLE 3. Demographic and Clinical Characteristics of Patients With HL According to HIV Status

Clinical Characteristics	HIV-Positive No. (%)	HIV-Negative No. (%)	95% CI	*P*
HL subtypes				.219
MCCHL	6 (12)	44 (88)		
NSCHL	3 (10)	27 (90)		
LRCHL	2 (50)	2 (50)		
LDCHL	0	2 (100)		
NLPHL	1 (20)	4 (80)		
Stage of the disease				.485
Stage I	4 (15.4)	22 (84.6)		
Stage II	3 (12)	22 (88)		
Stage III	1 (5.3)	18 (94.7)		
Stage IV	3 (23.1)	10 (76.9)		
Early stage	3 (12.5)	21 (87.5)		
Advance stage	9 (13.4)	58 (86.6)		
Sex distribution			−0.05 to 0.28	.172
Male	6 (9.5)	57 (90.5)		
Female	6 (22.2)	21 (77.8)		
Age groups			−0.04 to 0.22	.331
≤ 14 years	2 (7.1)	26 (92.9)		
> 14 years	10 (15.9)	53 (84.1)		
WBC count × 10^3/μL			0.07 to 0.67	.005
≥ 3.98	7 (8.8)	73 (91.3)		
< 3.98	5 (45.5)	6 (54.5)		
Lymphocyte count × 10^3/μL			−0.007 to 0.26	.069
≥ 1.18	3 (6.7)	42 (93.3)		
< 1.18	9 (19.6)	37 (80.4)		
Monocyte count × 10^3/μL			0.04 to 0.34	.013
≥ 0.24	3 (5.6)	51 (94.4)		
< 0.24	9 (24.3)	28 (75.7)		
Hemoglobin, g/dL			−0.22 to 0.10	.51
≥ 11.2	5 (17.2)	24 (82.8)		
< 11.2	7 (11.5)	54 (88.5)		

Abbreviations: HL, Hodgkin lymphoma; CHL, classical Hodgkin lymphoma; LDCHL, lymphocyte-depleted CHL; LRCHL, lymphocyte-rich CHL; MCCHL, mixed-cellularity CHL; NLPHL, nodular lymphocyte-predominant HL; NSCHL, nodular sclerosis CHL.

75.8%, and 66.7%, respectively (Appendix Fig A3). Among patients with advanced-stage disease, the 4-year OS among the high-risk group of patients (IPS ≥ 3) was numerically lower than in the low-risk group of patients (IPS ≤ 2), 68.9% and 93.3%, respectively, but there was no statistically significant difference between the two groups (P = .177) (Fig 2).

As depicted in Table 4, LDCHL, the most aggressive HL subtype, was associated with a 3-year OS rate of 50%, whereas MCCHL and NSCHL were associated with 4-year OS rates of 86.5% and 89.9%, respectively. Patients with the NLPHL subtype exhibited 100% 4-year survival rate. Patients with lymphocyte count of ≤ 0.6 × 10^3/μL had a poor 4-year OS rate (70.8%) and this was the only prognostic factor with significant impact on OS. Patients treated with combined chemotherapy/radiotherapy exhibited excellent survival, with a 4-year OS of 100%, whereas for patients receiving ABVD only, the 4-year OS was 77.9% (Appendix Fig A4). Only 5 HL patients with HIV were included in the survival analysis, and all were alive up to the last date of follow-up data collection.

DISCUSSION

HL has shown differences in age distribution and histopathologic subtypes in different geographical, genetic, and environmental settings.[30] In high-income countries, HL shows a bimodal age distribution at diagnosis.[4,31] By contrast, our study showed more cases among the younger age group, and was rare among the elderly. This is partly explained by the differences in demographic distribution, which is characterized by large proportion of younger age group and consequently, HL significantly decreased after the age of 50 years. Our finding is similar to what reported from other low-income countries.[5-7,32]

Several risk factors have been related to HL such as sex, age, race, and genetic and environmental factors.[4,31] Male sex has been stated as a risk factor for contracting HL.[33] Moreover, the incidence rates of HL has been found to be higher in males more than in females of all races.[34] Similarly, in this study, the incidence of HL was higher in males compared with females. However, the male-to-female proportion of HL cases in Ethiopia was relatively higher than in developed countries,[31,35] and was lower than what has been reported from other sub-Saharan African countries.[5,6] In addition, HIV has been suggested as a risk factor for developing Hodgkin lymphoma.[36] A recent study assessed the impact of HIV epidemic on the increasing incidence of cancer in sub-Saharan Africa and reported 8.6% of cases to be associated with HL.[37] Likewise, our study has detected a relatively high proportion of HIV-associated HL (13%). This finding is 3-fold higher than that reported in the United States.[38]

The majority of HL cases in this study (65.8%) were categorized as stage I and II at diagnosis. This is in contrast to a study conducted in Nigeria, which reported a predominance of late stages.[5] Furthermore, our finding showed that 63.7% of patients with HIV-associated HL presented with early stages at diagnosis. This is consistent with a study reporting that patients with HIV were more likely to present at early stages of any type of cancer compared with the general population in Africa.[37]

In HL, the hemoglobin level and peripheral WBC count and composition are important prognostic factors at diagnosis and at treatment evaluation, and are part of the IPS for

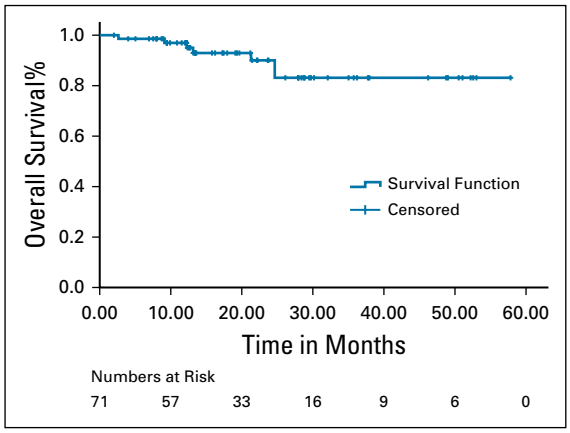

FIG 1. OS of patients with HL. The 4-year OS was 83.1%. HL, Hodgkin lymphoma; OS, overall survival.

patients with advanced-stage disease. In this study, 65.1% of HL cases presented with low hemoglobin and most WBC compositions also were low in the majority of cases. Similarly, 53% of patients with HL were found to be anemic in a study conducted in Pakistan.[39]

The dominant HL subtypes in this study was MCCHL (50.4%), consistent with findings from Kenya (44.9%)[6] and lower than reported from Nigeria (64.3%).[5] However, the second dominant subtype was NSCHL in our study, which is different from the finding from Kenya and Nigeria, in which NLPHL was the second dominant subtype.[5,6] By contrast, a recent study from Egypt has reported NSCHL as a common subtype of HL.[32] Previous studies from the United States and Europe indicate the NSCHL subtype to be the dominant subtype.[34,40] This discrepancy might be because of differences on environmental factors and exposure to infections.[17,41] Most HIV-positive HL cases were MCCHL subtypes followed by NSCHL. Our finding is similar to the report of a study from South Africa.[42] Several reports suggest the possible association of MCCHL subtype of HL with viral infection, especially of Epstein-Barr Virus.[18,41]

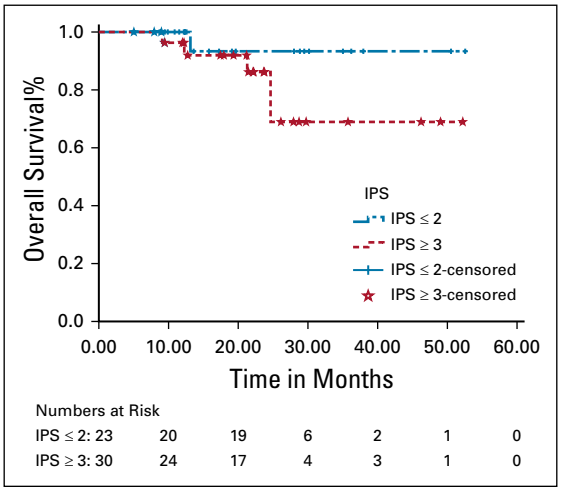

FIG 2. OS of patients with HL in the low-risk (International Prognostic Score [IPS] ≤ 2) and high-risk (IPS ≥ 3) groups. The 4-year OS was 93.3% and 68.9% for patients with IPS ≤ 2 and IPS ≥ 3, respectively. HL, Hodgkin lymphoma; OS, overall survival.

To our knowledge, this is the first study conducted to evaluate survival and prognostic factors of patients with HL in Ethiopia. The 4-year OS was estimated to be 83.1%, although median time of follow-up was relatively short, 19 months. This is similar to that reported from Malawi, with a 1-year OS rate of 83%,[43] and Nigeria, which reported an OS rate of 84.3%.[44] A study from Turkey reported a 10-year OS of 84%,[45] and others from the United States and the Nordic countries reported a 5-year relative survival ratio of 80%.[34,46] In Ethiopia, the standard first-line treatment regimen for HL is ABVD. However, the 4-year OS of patients who received ABVD only was 77.9%, a result which is similar to what was reported by Santoro et al,[47] but lower than reported in other populations (88%-90%).[45,48] By contrast, the group of patients with HL that received combined chemotherapy only or received combined chemotherapy followed by radiotherapy showed an excellent outcome in this study.

In this study, we were able to confirm the prognostic impact of the IPS. In our series, however, the strongest prognostic factor was lymphocytopenia. Generally, MCCHL and LDCHL are considered to be the HL subtypes associated with worst survival outcome, and NLPHL subtype has a good prognosis and survival outcome.[49] In this study, the impact of histopathologic subtype could partly be confirmed. LDCHL was associated with the most inferior outcome, followed by MCCHL and NSCHL, but all patients with NLPHL were long-term survivors.

Our study has several limitations. It is a hospital-based retrospective study and the sample size was relatively small, which may affect the strength of the findings. As the study included only cases who attended or were referred to TASH during the study period, bias issues concerning the number of patients who are treated at TASH compared with the patients who did not get access for diagnosis and treatment may be raised. Another limitation of the study was the lack of an organized cancer and death registry system in Ethiopia, which may underestimate the rate of disease progression and lymphoma-related deaths. The median follow-up time is also short, <2 years.

In conclusion, the populations at risk for HL in Ethiopia are adolescent and young adults, and the risk of HL declined gradually in older ages. In general, the treatment outcome for the patients included in this series was favorable and comparable to that of other populations, including in HIV-infected individuals. Our results showed that even in a low-resource setting, excellent treatment outcomes can be achieved after appropriate diagnostic workup and standard chemotherapy. The majority of HL

TABLE 4. OS and Prognostic Factors

Characteristics	1-Year OS%	2-Year OS%	3-Year OS%	4-Year OS%	*P*
OS	97.0	90.0	83.1	83.1	
IPS					.177
IPS ≤ 2	100	93.3	93.3	93.3	
IPS ≥ 3	96.3	86.2	68.9	68.9	
Sex					.746
Male	97.4	91.2	80.5	80.5	
Female	96.0	87.3	87.3	87.3	
Age group					.4
0-9	91.7	91.7	91.7	91.7	
10-19	94.1	83.7	83.7	83.7	
20-29	92.9	74.3	49.5	49.5	
> 30	100	90	90	90	
Ann Arbor staging					.654
Stage I	94.1	94.1	94.1	94.1	
Stage II	94.1	76.3	76.3	76.3	
Stage III	—	90.9	75.8	75.8	
Stage IV	—	—	66.7	66.7	
Early and advanced stages					
(Stage I and IIA) early stage				100	.140
Advanced stage (stage I and IIB, III, and IV)	96.1	87.4	78.2	78.2	
HL subtypes					.721
MCCHL	96.2	86.5	86.5	86.5	
NSCHL	96.3	89.9	89.9	89.9	
LDCHL	100	50	—	—	
LRCHL	—	—	—	—	
NLPHL	100	—	—	—	
WBC count					.069
WBC > $10.04 \times 10^3/\mu L$				100	
WBC ≤ $10.04 \times 10^3/\mu L$	95.4	92.6	85.3	76.3	
Lymphocyte × $10^3/\mu L$					.015
> 600	100	100	100	100	
≤ 600	94.3	82.6	70.8	70.8	
Monocyte × $10^3/\mu L$					.078
> 0.24	100	94.7	88.8	88.8	
< 0.24	91.8	82.8	74.5	74.5	
Hemoglobin, g/dL					.772
≥ 10.5	100	91.7	91.7	91.7	
< 10.5	97.7	91.4	83.1	83.1	
Treatment					.112
ABVD only				77.9	.112
ABVD plus				100	

Abbreviations: ABVD plus, patients treated with combined chemotherapy ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine) and COPDAC (cyclophosphamide, vincristine sulfate, prednisone, and dacarbazine) or radiotherapy; CHL, classical Hodgkin lymphoma; HL, Hodgkin lymphoma; IPS, International Prognostic Score; LDCHL, lymphocyte-depleted CHL; LRCHL, lymphocyte-rich CHL; MCCHL, mixed-cellularity CHL; NLPHL, nodular lymphocyte-predominant HL; NSCHL, nodular sclerosis CHL; OS, overall survival.

cases in this study were from regions near to Addis Ababa, and very few from more distant regions, indicating that most of the population of the country were not able to get access to cancer medical services, which is the main obstacle for improving the outcome for patients with HL in Ethiopia.

AFFILIATIONS

[1]Department of Microbial, Cellular and Molecular Biology, College of Natural Sciences, Addis Ababa University, Addis Ababa, Ethiopia
[2]Armauer Hansen Research Institute, Addis Ababa, Ethiopia
[3]Department of Oncology, Faculty of Medicine, Lund University, Lund, Sweden
[4]Yirgalem Medical College, Yirgalem, Ethiopia
[5]Department of Pathology, College of Health Sciences, Addis Ababa University, Addis Ababa, Ethiopia
[6]Department of Internal Medicine, College of Health Sciences, Addis Ababa University, Addis Ababa, Ethiopia
[7]Department of Oncology and Pathology, Karolinska Institute, Stockholm, Sweden

CORRESPONDING AUTHOR

Makka Adam, Armauer Hansen Research Institute, Jimma Rd, PO Box 1005, Addis Ababa, Ethiopia; e-mail: mekaali@yahoo.com.

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AUTHOR CONTRIBUTIONS

Conception and design: Makka Adam, Yonas Bekueretsion, Abdulaziz Abubeker, Fisihatsion Tadesse, Rawleigh Howe, Beyene Petros, Mats Jerkeman, Amha Gebremedhin
Financial support: Mats Jerkeman
Administrative support: Beyene Petros
Provision of study materials or patients: Yonas Bekueretsion, Fisihatsion Tadesse, Amha Gebremedhin
Collection and assembly of data: Makka Adam, Yonas Bekueretsion
Data analysis and interpretation: Makka Adam, Abdulaziz Abubeker, Anna Kwiecinska, Beyene Petros
Manuscript writing: All authors
Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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APPENDIX

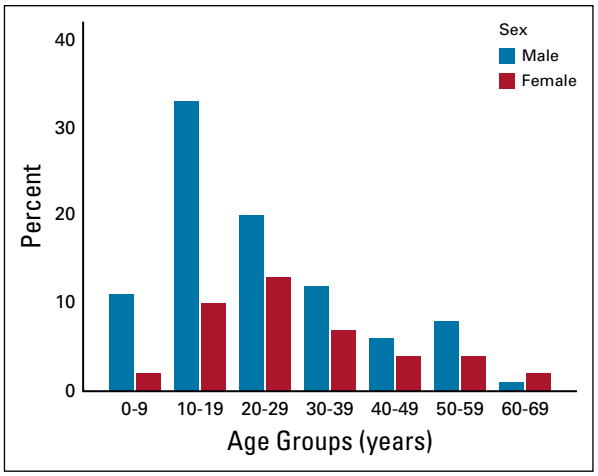

FIG A1. Age and sex distribution of patients with Hodgkin lymphoma during the study period.

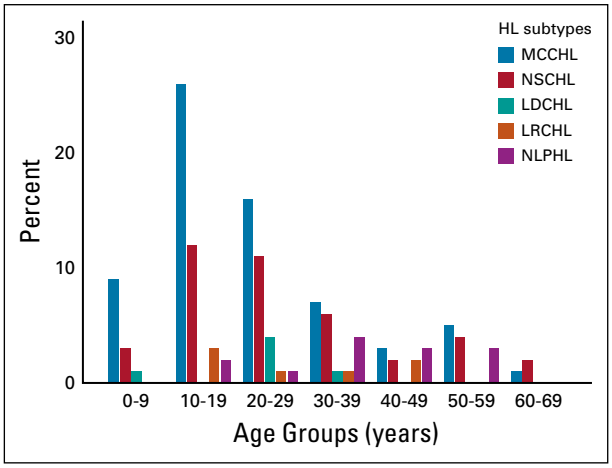

FIG A2. HL subtypes among different age groups during the study period. CHL, classical Hodgkin lymphoma; HL, Hodgkin lymphoma; LDCHL, lymphocyte-depleted CHL; LRCHL, lymphocyte-rich CHL; MCCHL, mixed-cellularity CHL; NLPHL, nodular lymphocyte-predominant HL; NSCHL, nodular sclerosis CHL.

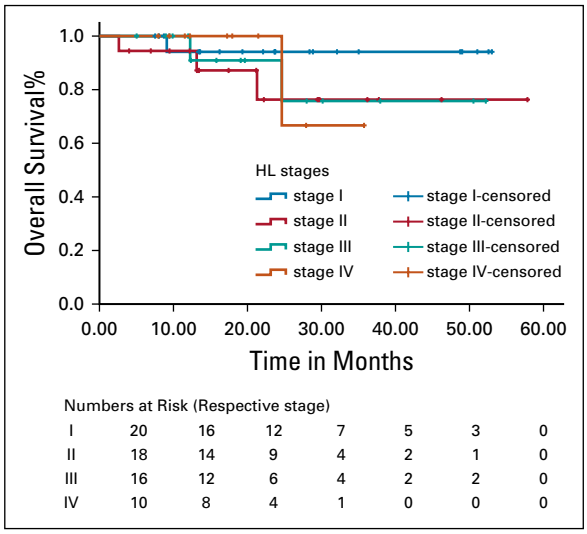

FIG A3. Overall survival of patients with HL at different stages of the disease. The 4-year OS was 94.1%, 76.3%, 75.8%, and 66.7% for stage I, stage II, stage III, and stage IV, respectively. HL, Hodgkin lymphoma.

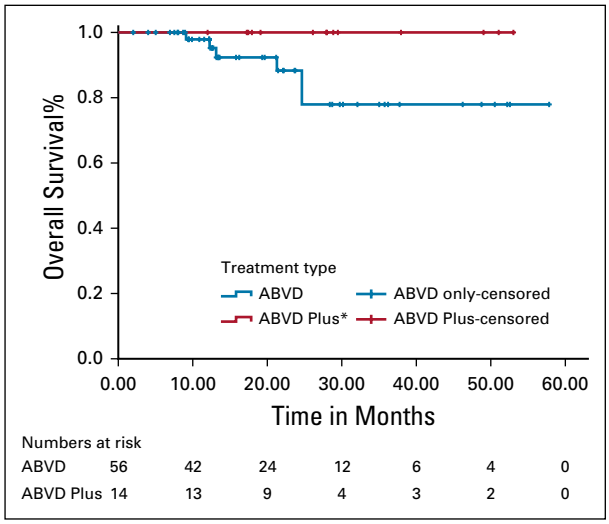

FIG A4. Four-year overall survival of patients with HL who received different treatment regimens. The 4-year OS was 77.9% and 100% for patients received ABVD only and those received ABVD and COPDAC/radiotherapy (ABVD Plus), respectively. ABVD plus, patients treated with combined chemotherapy ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine) and COPDAC (cyclophosphamide, vincristine sulfate, prednisone, and dacarbazine) with or without radiotherapy; HL, Hodgkin lymphoma.

TABLE A1. Distribution of Patients With HL in Ethiopia During the Study Period

Permanent Residence	No.	%	Population
Addis Ababa	34	27.9	3,434,000
Amhara	27	22.1	21,134,988
Dire Dawa	1	0.8	466,000
Harari	1	0.8	246,000
Oromia	43	35.2	35,467,000
SNNPR	12	9.8	19,170,007
Somali	1	0.8	5,748,998
Tigray	3	2.5	5,247,005
Total	122	100.0	

Abbreviations: HL, Hodgkin lymphoma; SNNPR, South Nations Nationalities and Peoples of Ethiopia region.

TABLE A2. Proportion of Hodgkin Lymphoma Subtypes Among Sex and Age Groups

	HL Subtypes									
	MCCHL		NSCHL		LRCHL		LDCHL		NLPHL	
	No.	%	No.	%	No.	%	No.	%	No.	%
Sex										
Male	49	73.1	23	57.5	6	85.7	4	66.7	9	69.2
Female	18	26.9	17	42.5	1	14.3	2	33.3	4	30.8
M:F ratio	2.6:1		1.2:1		6:0		2:1		2:1	
Age group										
0-9	9	13.4	3	7.5	0	0.0	1	16.7	0	0
10-19	26	38.8	12	30	3	42.9	0	0	2	15.4
20-29	16	23.9	11	27.5	1	14.3	4	66.7	1	7.3
30-39	7	10.4	6	15	1	14.3	1	16.7	4	30.8
40-49	3	4.5	2	5	2	28.6	0	0	3	23.1
50-59	5	7.5	4	10	0	0.0	0	0	3	23.1
60-69	1	1.5	2	5	0	0.0	0	0	0	0

Abbreviations: CHL, classical Hodgkin lymphoma; HL, Hodgkin lymphoma; LDCHL, lymphocyte-depleted CHL; LRCHL, lymphocyte-rich CHL; MCCHL, mixed-cellularity CHL; NLPHL, nodular lymphocyte-predominant HL; NSCHL, nodular sclerosis CHL.

