PATTERNS OF HODGKIN'S LYMPHOMA: EPIDEMIOLOGY, CLINICAL PRESENTATION, HISTOLOGIC SUBTYPES, PROGNOSTIC FACTORS, AND TREATMENT OUTCOME IN TASH from December 2010 to December 2015

A Research Project submitted to Department of Internal Medicine, School of Medicine, College of Health Sciences, Addis Ababa University for the partial fulfillment of internal medicine Specialty Certificate

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SUMMARY PAGE

PROJECT TITLE

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THEMATIC AREA: Hematology Unit, TASH, AAU,CHS, AA Ethiopia

SUB-THEMATIC AREA: Hodkins Lymphoma

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FULL TITLE OF THE PROJECT

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Acronyms

ABVD Doxorubicin, bleomycin, vinblastine, dacarbazine

ASCT Autologous stem-cell transplantation

BEACOPP Bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, Procarbazine, prednisone

cHL Classical Hodgkin lymphoma

CR Complete remission

CS Clinical stage

COPP Cyclophosphoamide, vincristine, procarbazine, prednisone

EBV Epstein-Barr virus

EFS Event-free survival

IFRT: Involved field radiotherapy

IPS International Prognostic Score

HD: Hodgkin's Disease

HL: Hodgkin's lymphoma

LDHL Lymphocyte depleted Hodgkin lymphoma

LRCHL Lymphocyte rich classical Hodgkin lymphoma

MCHL Mixed cellularity Hodgkin lymphoma

NHL NonHodgkin's lymphoma

NLPHL Nodular lymphocyte predominant Hodgkin lymphoma

NSHL Nodular sclerosis Hodgkin lymphoma

PD Progressive disease

PR Partial response

PS Pathological stage

TASH Tikur Anbesa Specialized Hospital

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Abstract

Background:

Hodgkin lymphoma (HL) exhibits considerable clinico pathological variations in different parts of the world. This study was prompted by the limited availability of HL data in developing countries (particularly long-term outcomes).

Methodology:

This is hospital based retrospective study of 96 patients diagnosed and treated with HL at TASH, from December 2010 to December 2015, at department of internal medicine, hematology unit. Patient records and phone interviewing was used to collect data.

Results:

The study included 96 patients with a median age of 24 years (range14–60 years); 58% of patients were between ages 14-25. 71 % were male, male to female ratio of 2.4. The most common primary presentation was peripheral lymphadenopathy (93%), the neck lymph nodes were primary complaints in 75% of patients. B symptoms occurred in 63% .71% had an advanced stage, 25% had bulky disease. Mixed Cellularity was the most common histological subtype (52%). Initial therapy outcomes were complete response, progressive disease, partial response, and in 84%, 8%, and 7% of patients, respectively. The mean follow up patients from patient records was 12 months, from phone interviews 36 months. The 5 year overall survival (OS) 81%., and progression free survival (PFS) was and 70%.Multivariate analysis showed that treatment discontinuation was independently associated with death.

Conclusion:

Hodgkin's Lymphoma follows epidemiological and clinical features of developing countries at our center. The 5-year overall and progression-free survivals were below international rates. Treatment adherence significantly contributes to overall survival.

Key words; Hodgkin's Lymphoma, clinical pattern, survival analysis, Ethiopia.

Background

Hodgkin's lymphoma is a lymphoid malignancy characterized by tumoral growth of the lymph nodes that consists of the rare neoplastic Reed-Stenberg cells on the background of polyclonal inflammatory infiltrates [8, 12]. It has two basic types based on the appearance and immunophenotype of the tumor cells in to classical HL and nodular lymphocyte predominant HL[13,12]. Classical form is also further subdivided into nodular sclerosis (NS), mixed cellularity (MC), lymphocyte predominant (LP), lymphocyte depleted (LD)[15].

Hodgkin lymphoma (HL) accounts for approximately 10 percent of all lymphomas and approximately 0.6 percent of all cancers diagnosed in the developed world annually (1).It is an uncommon tumor. It occurs in 2-3 per 100,000 populations in developed countries [1-3]. Incidence pattern of HL is influenced by age and geographic location [13]. In developed countries, there is one peak in young adults (approximately age 20 years) and one in older age (approximately age 65 years); the majority of patients are young adults [10, 11]. In developing countries, there is an initial peak in childhood for boys, relatively low rates in young adults, and a late peak in older adults [15-17]. HL Shows a slight male predominance [1-3, 6].

The predominant histologic subtype also differs by geographic location and economic advancement. In developed countries such as the US, nodular sclerosis HL (NSHL) is the predominant histologic subtype and accounts for most of the peak in young adults. In economically disadvantaged areas, mixed cellularity HL (MCHL) is more frequent in children and older adults. Early industrialized or transitional economies tend to have an equal frequency of MCHL and NSHL subtypes. Approximate relative proportion of each subtype in western countries is reported as Nodular sclerosis classical HL (70 percent) Mixed cellularity classical HL (20 to 25 percent) Lymphocyte rich classical HL (5 percent) Lymphocyte depleted classical HL (less than 1 percent) [10-16].

Risk factors for HL are socioeconomic status, immunosuppression like HIV; HIV increases the incidence of HL. The relative risk is reported variably from five to 25. The incidence of HL in HIV is not correlated with degree of immunosuppression, as opposed to NHL; it can occur at any level of CD4 count and commonly with moderate CD4 count depression [19-21].

The typical patient with HL is a young adult who presents with enlarged lymph nodes in the neck and chest X-ray often reveals an enlarged mediastinum. Also, abdominal glands may be involved as well as extranodal sites, the most common being bone marrow and lungs [26-27].

The treatment of patients with Hodgkin lymphoma (HL, formerly called Hodgkin's disease) is primarily guided by the clinical stage of disease as determined by the Cotswolds classification. The advent of multi-agent chemotherapy and improved approaches to radiation therapy have led to HL being one of the most curable malignancies with long-term survival rates above 90% in early-stage disease. Over the past century, HL has been converted from a uniformly fatal disease to one that is curable in approximately 75 percent of patients worldwide [42-45].

Statement of the problem

Treatment and outcome of Hodgkin lymphoma (HL) are generally satisfying .There outcome were generally remarkable in the last few decades of HL with the advent of better understanding of the biology of disease, staging techniques, treatment involving multidiscipline of modern medicine and tailoring of treatment.

The outcome of HL in developed countries from the cancer registries is widely available. Data from developing countries is very little [36-39, 41]. There are no previous studies that tried to evaluate the long term outcome of patients with HL in our country. In this study we try to evaluate the epidemiology, clinical features and long term outcomes of patients with HL, treated over a period of 5 years at TASH, from December of 2010 to 2015.

OBJECTIVES

GENERAL OBJECTIVES

- To describe patterns of HL in TASH in the year 2010 to 2015
- To describe Outcomes HL treatment in TASH in the year 2010 to 2015

SPECIFIC OBJECTIVES

- To describe socio demographic characters of HL
- To describe clinical presentations of HL
- To describe Identified risk factors for HL
- To describe the proportions of different histological subtypes
- To describe prognostic factors of the HL

Method

This is a retrospective study based in TASH, a tertiary hospital at the capital of Ethiopia Addis Ababa, patients aged ≥14 years with a diagnosis of HL who received treatment at the hematology unit of TASH between Dec 2010 and December 2015 were identified from the hematology referral clinic logbook and chemotherapy dispensary registry of the same clinic as well as registries to the internal medicine wards of TASH.

Diagnosis and work up

The diagnosis of HL was made based on LN biopsy and histopathologic examination. Immunophenotypic study was done for only few patients. The patients records were retrieved from both chart and electronic records .Patients lost to follow up that were able to be traced by phone calls were traced to determine their current status.

Patients work up included clinical evaluation (history and physical examination), complete blood counts, and serology for Hep B and C, serology for HIV, renal and liver function tests, serum albumin, uric acid and serum lactate dehydrogenase. Two-dimensional echo was done when indicated.

Staging workup

Staging workup mainly included clinical examination, abdominopelvic US and a chest X-ray, few patients underwent CT scan, and bone marrow examination was done also for few patients. None of the patients underwent FDG-PET scan during initial or repeat staging, as the modality is not available.

The modified Ann Arbor Staging system was used for staging. Bulky disease was considered when the lymph node was 10 cm or more in size, or when the mediastinal mass occupied more than one-third of the chest diameter. B symptoms were defined as patient reported complaints of

fever, night sweating and significant weight loss that the treating physician labeled as B symptoms. ESR was considered to be elevated when it is more than or equal to 50 or when more than or equal to 30 with bulky disease, B symptoms, or both. Patients with stage I and stage IIA were considered as early stages and those with stages II-B, III, and IV were considered as advanced stages of the disease. Early stage disease with bulky disease or B symptoms was considered unfavorable prognosis.

Treatment

Treatment included CCT with general plan of 4-6 cycles for early disease and 6-8 cycles for late disease. Early stage HL (Stages IA, IB, and IIA) without unfavorable prognosis was initially planned for IFRT but all patients subsequently received 4-6cycles plan of ABVD chemotherapy. All the other patients were planned for 6-8 cycles of ABVD chemotherapy. None of the patients in these study received RT as initial single or combined treatment or as palliation.

Follow up and treatment response

Patients were reevaluated monthly or earlier (if indicated) for treatment response and toxicity. During each visit patients were clinically restaged for disease response. Proper restaging of patients was planned with imaging and seldom tissue based method after 4-6 cycles of chemotherapy. CT was used for few patients and PET wasn't done for any of the patients.
Response was were categorized as follows: complete response (CR), defined as complete disappearance of disease on radiography and normal bone marrow biopsy for previously positive cases; partial response (PR), defined as a $\geq$ 50% decrease in the diameter of measurable lesions; progressive disease (PD), defined as a $\geq$ 50% increase in the diameter of measurable lesions or the detection of new lesions; and stable disease (SD) defined as a failure to attain CR, PR or PD. *The treating team's decision of treatment response was taken*.

Overall survival (OS) was computed from the date of start of initial chemotherapy to the date of death from any cause on phone interviews or on patient records. Progression-free survival (PFS) was defined as time from start of treatment till relapse or PD, no CR at the end of first-line treatment, or death due to any cause, or loss to follow-up with disease. Phone interviews were only used to define if a patient is alive or dead, information about disease progression was only taken from patient record by physician evaluation of the last time patient was seen on follow up.

Data collection and data collecting instrument

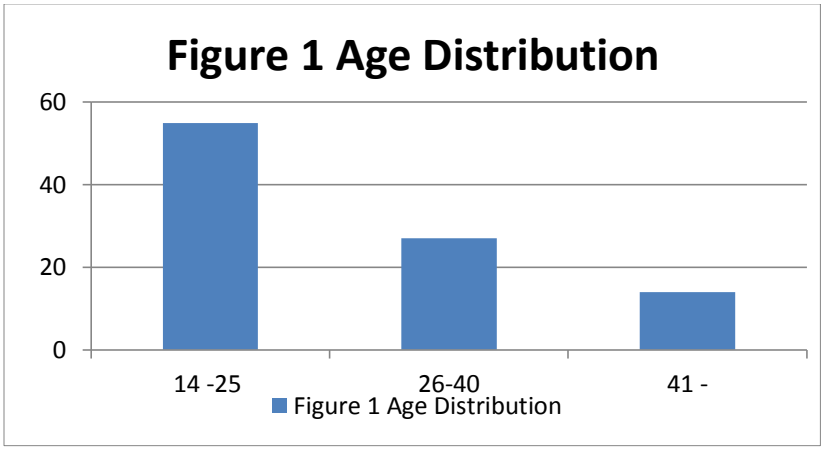
The data were collected using a pre tested data collecting tool that included patient demographics, clinical features, and laboratory work up, imaging and histopathology result, treatment and follow up information. Phone interviews were made from phone numbers registered on patient charts.

Patients records were obtained from both electronic and charts records were retrieved, patients lost to follow up that were able to be traced by phone calls were traced to determine their current status. Patients were asked for permission before phone conversations. The baseline line epidemiological and clinical data of patients was entered to *SPSS 20* and basic epidemiological and clinical data was analyzed using frequency function. *Multivariate analysis and the chi square* test were used to assess association with overall and progressive free survival. The survival analysis was done by using *Kaplan Meier curve* and associations were tested by using the log rank test.

Results

Demography

A total of 96 patients were analyzed 5in this study, of these 68(71%) were males and 28 (29%) were females. The male to female ratio is *2.42.* The median age for the study was 24(range 14-60). Most of the patients were from Addis Ababa (39%) followed by Oromia (28%). Most of the patients presented with nodal swelling with peripheral LAP (94%) and (4%) as internal LAP as primary presenting complaint.



	Male	Female	M: F
Age 14-25	41	14	2.9
Age 26-40	20	7	2.9
≥ 41	7	7	1
Total	68	28	**2.42**

Figure 2: Age distribution *Table 1: Age and sex distribution*

Histologic type of HL

Most patients (68%) presented with FNAC results to the referral clinic but in all patients but one the diagnosis was made on LN biopsy. Diagnosis was made by light microscopy; immunophenotyping was done for 2 patients.

Majority of the patients had classical HL (94%) with MC (52%), followed by NS (20%), LP (17%), and LD (2%). *Four patients had NLP HL*. In one patient the diagnosis of HL was made clinically after he presented with symptoms of cough and inaccessible mediastinal swelling and treatment was started on clinical grounds. (See figure 2 and table 2)

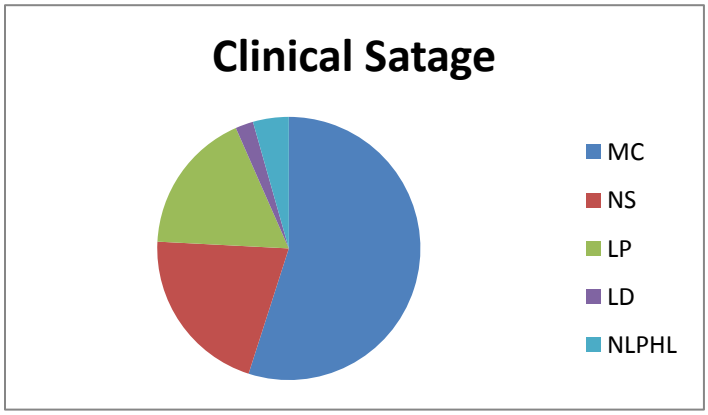


Figure 2: Histologic Types

	Male	Female	M: F
NS	9	10	0.9
MC	35	15	2.3
LP	15	1	15
LD	1	1	1
NLPHL	3	1	1
Unclassified	7	1	7
Total	68	28	

Table 2: Histology Vs. Sex

Clinical Features

The median duration of presentation before the illness was 12 months (range 2-72 months).
The neck lymph nodes were the major presenting feature in 75% of the cases. Mediastinal involvement was seen in 23% of the patients. Isolated infra diaphragmatic involvement was seen in only 4% of the patients.

Extranodal involvement was seen in 41% of the patients. The liver is the most commonly involved organ with 20% of patients, followed by the lungs or pleura 15(16%) patients, pericardium in 4(4%) patients, 3 patients had involvement of the bone and one patient had kidney involvement. All but two patients with extranodal involvements were diagnosed by imaging techniques and without tissue diagnosis, in the two patients one was diagnosed by post pneumenctomy biopsy and the other was diagnosed after laparotomy for acute abdomen.

Bulky disease was seen in 25% of patients and B symptoms were seen in the majority of patients (62.5%). Fever (51%) was the most common B symptom. About 38% of the patients received treatment as some other diagnosis before finally being diagnosed with HL, of these *TB (95%)* was the leading cause of misdiagnosis.

Only 8 patients didn't undergo screening for HIV, 19 patients (20%) were HIV positive, the remaining patients were sero-negative for HIV. For 16 out of the 19 HIV positive patients had their CD4 determined, the mean CD count was 234(range 50-600). The histologies in the HIV positive patients were MC (12), NS (4), LP (3). The histologic features in patients with HIV are MC/LP: NS, 15: 4. Among the 19 HIV positive patients 15 had followed up and on remission, 4 patients were lost to follow ups.

Staging was done clinically, it included B symptoms, ESR measurement (68%), abdominal US (100%) , chest imaging which included CXR in most, CT guided staging was done in 14 patients(15%), BM examination was done in 6 patients(6%), all showed no bone marrow involvement. PET scan wasn't available during the study period and none of the patients underwent PET scans. Majority of patients presented with advanced stage disease (71%).

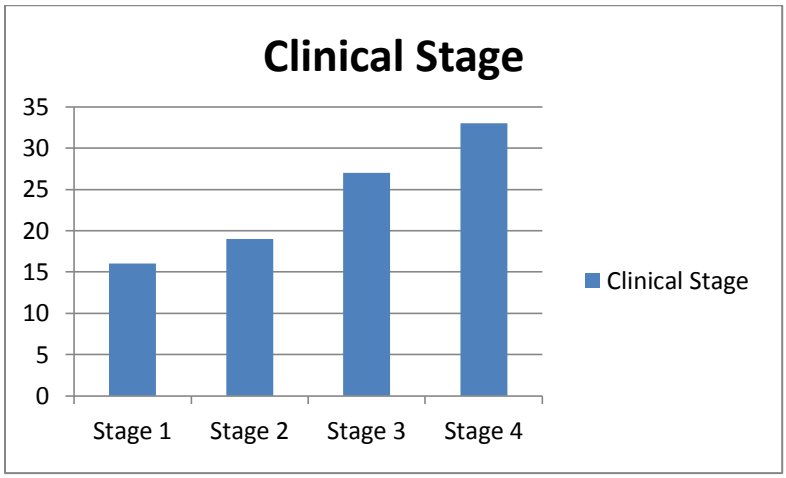


Figure3: Stage distribution

Table 3: Base line patient characteristics

Baseline characteristics						
Number (96)(100%)						
Gender	Male	68(71)				
	Female	28(29)	t(96)			
Age						
	14-25	55(58)				
	26-40	27(28)				
	41 and above	14(14)		Total 96		
Primary Site	Perip. LAP	89(93)				
	Internal LAP	4(4)				
	Extranodal	3(3)		Total 96		
Histologic Type						
	MC	50(52)				
	NS	19(20)				
	LP	16(17)				
	LD	2(2)				
	NSLPHL	4(4)				
	Unclassified	8(8)				
	Clinical	1(%)		T(96)		
Stage						
	IA	14(15%)		IIIA	5(5%)	
	IB	3(3%)		IIIB	22(23%)	
	IIA	8(8%)		IVA	2(2%)	
	IIB	11(12%)		IVB	31(32%)	T(96)
Stage Early/Late						
	Early	25(26)				
	Late	71(74)				
ESR						
	High	43				

	Low	22		t(65)		
B symptoms						
	Yes	60(63%)				
	No	36(37%)				
HIV						
	Positive	19(20%)				
	Negative	69(72%)				
	Unknown	8(%)		T(96)		
Treatment	ABVD	93(97%)				
	COP	1(1%)				
	ABVD/COP	2(2%)				
	IFRT	0(0%)		T(96)		
Tx Completed	Yes	79(82%)				
	No	17(18%)		T(96)		

Treatment

Ninety five of the ninety six patients received at least 2 cycles of chemo, one patient disappeared after day 1 of the first ABVD cycle. Three patients before 2012 received COPP-type regimens, one patient took COP only and two others ABVD/COP combination, standard ABVD chemotherapy was administered in remaining patients. None of the patients in these study received RT as initial single or combined treatment or as palliation. Patients who have taken less than physician prescribed courses or took courses but missing one of the components of CCT due to lack of availability or presumed toxicities were 18%, and they are considered as incompletely treated.

Treatment Outcome

The median period of follow up from patient records after treatment completion or default was *12.2 months*, with phone interviews the median treatment follow-up for survival increased to 36 months and PFS duration median to 17 months, *both durations used in the survival follow up started from treatment initiation*.

A total of 89 patients received at least four cycles of chemotherapy of these 77(87%) achieved CR with induction chemotherapy, PD and PR each had 6 patients (6.6%). Of the 7 patients who took less than four cycles of chemotherapy 6 patients were lost to follow up and one patient died after the third cycle.

At a median follow up of 36 months (range from 0- 96) both from patient record and phone interviews, 84(88%) patients were alive. Twelve patients have died, two have died in hospital with progressive disease and sepsis, the rest 10 patients were traced by phone interviewing of the relatives, and the time from initiation of chemo to the patient's death date was used to calculate the overall five year survival.

Of patients with primary refractory disease two patients were referred abroad for ASCT one is alive after 48 months and the other died few months after the ASCT. Of the remaining 10 patients one patient was tried with repeat ABVD cycles as she has discontinued the previous cycle at fourth cycle, she had a resistant disease and later died after few months; the rest couldn't afford the salvage chemotherapy and were dead (5) or lost to follow-up. and couldn't be reached through the phone, one patient was alive at 48 months.

A total of eight (8.9%) patients who had been on remission after at least 4 cycles of chemotherapy developed relapse. Early remission was diagnosed in most of them (5). Of the patients with early remission only one patient received salvage chemotherapy as GCD at the oncology center, she later died of progressive disease. The rest four patients couldn't afford salvage chemotherapy and they were either lost to follow up (2) or dead (2) (*traced through phone interview*). Patients with late remission were three, one was lost to follow up, and one died after failing repeat ABVD induction and one patient achieved 2nd remission and was alive at 34 months.

Response and Disease Outcome

The 5-year overall survival (OS) and progression free survival (PFS) rates of our study were 81% and 70 %, respectively (Fig). The estimated 5 year OS of patients who have taken full dose/course of chemotherapy including a patient that died on 3rd cycle of chemotherapy was 87%. On multivariate analysis completing of full course of initial chemo was significantly associated with OS (P 0.00, HR 5.39(95% CI 1.22-23.7). Other predictors of outcomes on multivariate analysis didn't show significant associations (see table).

	n	%
n	96	
Discontinued treatment before 4 cycles	6	
Treatment response		
CR	76	84
PR	6	7
PD	7	8
SD	0	0
Completed whole course and dose of chemo	79	82
Disease relapse	8	9
Death	12	12.5
Predicted 5 year OS(±SE)	81 ± 5.2%	
Predicted 5 year PFS(±SE)	70 ± 7.5 %	

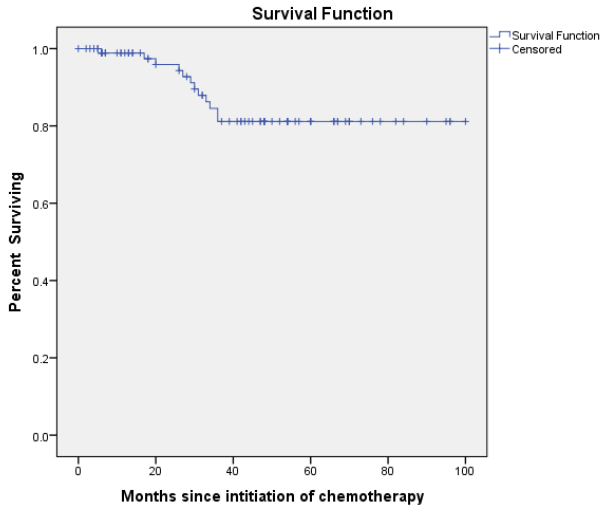
Table 4: Treatment and outcomes

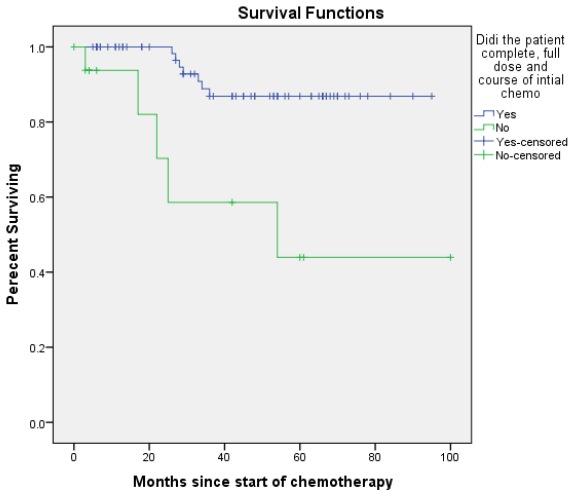
Variable	n(96)	P value	HR 95% CI
Sex			
Male	58(10)	0..36	0.46 (0.09-2.44)
Female	38(2)		
Age			
≤18	19(3)	0.92	1.08(0.24-7.73)
>18	65(9)		
B symptoms			
Yes	60(11)	0.09	0.15(0.17-1.3)
No	36(1)		
Stage			
Early	27(2)	0.35	0.21 (0.019-2.3)
Late	69(10)		
Extranodal involvement			
Yes	35(5)	0..4	0.56 (0.15-2.13)
No	61(7)		
LDH			
≥500	33(8)	0.065	0.07 (0.133-2.025)
<500	39(3)		
Completion of full induction			
Yes	72(7)	**0.026**	5.38(1.2-23.7)
No	12(5)		

Table 6: Predictors of outcome on multivariate analysis

Variables	5 year OS	
	Rate (%)	P value(log rank)
Age		
≤25	85	
>25	79	0.58
Sex		
Male	86.6	
Female	76.6	1.51
Histology MC Vs. NS		
MC	82.1	
NS	91.7	0.4
B symptoms		
Present	72.3	
Absent	94.1	0.016
Bulky Disease		
Yes	77.4	0.542
No	81.7	
Stage Early Vs. Late		
Early	88.2	0.201
Late	77.6	
LDH level		
≥500	63.6	
<500	88.4	0. 39
Extranodal Involvement		
Yes	71.8	
No	87.8	0. 2
Completion of full course of chemo		
Yes	86.9	
No	43.9	**0.00**

Table 6: Predictors of outcome on log rank test





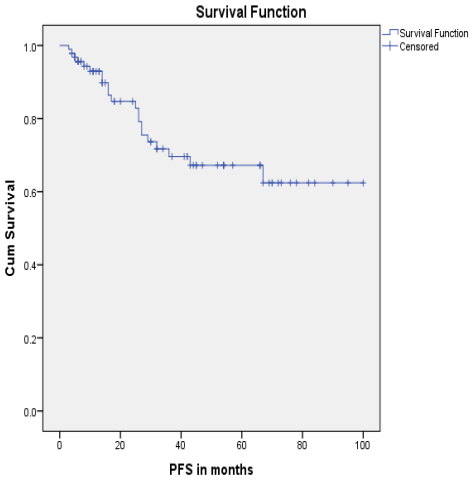


Figure 2A

Figure 4: Kaplan Meier Curves of overall survival, 5-OS treatment completed Vs Incomplete, 5 year PFS

Discussion

Demography

There are variations in the epidemiologic and clinico-pathological characteristics of HL in relation to geography and socioeconomic status [1, 10, 11]. In our study the median age was 24 years with 58% of patients between 14 and 25 years of age. There was no second peaking seen after the age of 60. This is consistent with the epidemiology in developing countries [36-40, 15-17] and this is different from the data in the west with average median age reported to be 34, with a bimodal peak, one in early 20s and a second peak seen after the age of 60 [1-3].

Hodgkin's Lymphoma is predominantly a disease of males, in our study 71% (m: f 2. 42) of the patients were male which is higher with the epidemiology reported from developed [1-3] and consistent with African [28-30, 40] and a review in our country [6].

Clinical Features at presentation

The mean and median duration of symptoms before the start of chemotherapy in this study was 16 and 12months, range 2 to 72 months. Which is much higher than the one reported from developed countries[1-3] Majority of the patients in this study presented with peripheral LAP as the primary complaint (89%) of which neck lymphadenopathy was the most common (58%). Several studies reported results consistent with this finding [42-45, 36-39].

In this study 62.5% of patients presented with B symptoms which is consistent with studies from developing countries, but much higher than the studies from developed countries (≤20). A higher proportion of patients (75%) had Stages III and IV disease, which is consistent with studies from other developing regions of the world [40, 42-45, 36-39], and higher than that reported in US SEER data (36%) and other developed parts of the world.

These adverse prognostic features at initial presentation in the present study possibly could be due to delay in presentation. *Mis diagnosis could potentially explain this feature as 38% of patients were initially misdiagnosed and have received treatment as something else, of these 95% had been misdiagnosed as tuberculosis before. Greater reliance on clinical judgment and aspirates than tissue diagnosis as 68% patients presented with FNAC might have contributed to the misdiagnosed cases. This pattern of presentation also occurs in other African countries*[40, 42-45]

Twenty two percent of patients in this study were diagnosed with HIV, among the screened patients, which is higher than other population based studies. The reason could be the greater health system contacts HIV positive patients have. The average CD4 count of the patients which was 234 is consistent with the pattern of HL in moderately immune suppressed HIV patients [19-21].

Histology

Several studies in both affluent and resource limited parts of the world reported the most common form of HL is classic form (about 95%) and lymphocyte – predominant form is rarely seen (5%), this is consistent with the 96% Vs. 4%, result seen in our study[1-3, 10,16]. Fifty two percent of patients had MC histology, a figure similar to reports from countries with limited resources [40, 28-30], but different from developed nations where nodular sclerosis type is reported to be the commonest [10-16]. This finding may indicate that the etiological role of Epstein-Bar virus (EBV) infection in the pathogenesis of HL, which is reported in the developing and communities with poor socioeconomic status [54-58]. In this study the proportion of Nodular sclerosis variant was higher in females than males, which is consistent with studies in both developed and developing parts of the world [1-3, 40] . HIV positive patients (22%) patients in this study none had LD histologic feature but most of them (15/19) had MC/LP, these histologic feature are predominant even in developed countries [59,60].

Outcome

Out of the total ninety six patient records retrieved, eighty two percent completed initial course of chemotherapy, the rest of the patients were lost to follow-up after starting chemotherapy, patients who took at least four cycles of chemo before being lost to follow up were eleven percent of patients, seven percent (6) of patients took less than four courses before being lost to follow-up. This pattern was described also in some developing countries where up to 15-20% loss to follow up were seen [36,40].

The CR rate after initial chemotherapy was 86% which is proportional to the figures reported from low resource setups but is slightly lower than figures from developed countries [39,45]. The 5-year overall survival (OS) (median follow up 36 months) and progression free survival (PFS) (median follow up 17 months) were 81% and 70%, respectively (Fig 1A and 2A).

The survival figures of the current cohort are relatively low. The 5-year OS rate and PFS rate were 81and 70%, respectively, which is lower in comparison to the survival figures of many developed regions [45-50], and some developing countries [39, 45] . Several trials have demonstrated an overall survival (OS) of >95% [61-65], and in late disease 5 year OS, >94% [61-65%].

Among the many factors associated with this we have determined that treatment default was significantly associated with OS on multivariate analysis. This problem has been reported by other developing countries [28, 40, and 66].

Other factors that have possibly contributed to the lower survival rate of our HL patients late presentation with advanced disease, with adverse prognosis features, even though in this study adverse prognosticators weren't significantly associated with outcome the number of the patients included in the study are low and thus lacks power to identify such indicators. The lack of PET scan directed management and single modality of treatment could have possibly resulted in poorer prognosis. Despite the presence of a radiation therapy unit in TASH none of our patient in these series received RT or CRT. Although these could be a result of sampling bias as TASH has a

separate oncology unit that treats patients with HL, others factors could have possibly contributed to low RT use. The radiation therapy unit was the only facility of its kind in Ethiopia, and it was flooded with patients. Preference often was given to those in whom no alternative effective therapy was available. The absence of government covered free salvage chemotherapy and the poor socioeconomic status of the patients explains why most patients with resistant disease failed to take salvage chemotherapy, in addition there is no HSCT service in our country.

Conclusion

The epidemiology of patients with HL at TASH follows the epidemiology seen in most developing countries. The CR rate for patients who have completed induction chemo is comparable to other developing countries, but 5 year OS is inferior to that seen in developed countries and some developing countries. **Treatment adherence** was significantly associated with overall survival.

Recommendations

We recommend having a larger study on the factors contributing to treatment adherence and for the HRC clinic to have a way of tracing of patients who default treatment. With the future expansion of RT services we hope to use more routine combined multimodal, response targeted therapy.

Limitation of the study

The card retrieval rate of this study was 50% making the sample size population low. Since the study is a retrospective study important information such as the IPS scores of advanced stage patients were missing in most of the patients and couldn't be used to evaluate the long term effect.

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