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*NON-HODGKIN'S LYMPHOMAS AT THE KENYATTA NATIONAL HOSPITAL, NAIROBI IN THE 1990's

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NON-HODGKIN'S LYMPHOMAS AT KENYATTA THE NATIONAL HOSPITAL NAIROBI IN THE 1990's

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ABSTRACT

Objectives: **To determine the clinico-pathologic and prognostic factors, treatment and outcome of non-Hodgkin's lymphomas as seen at the Kenyatta National Hospital in the 1990s.**

Design: **Retrospective study of patients with non-Hodgkin's lymphoma.**

Setting: **Kenyatta National Hospital, Nairobi, Kenya, between January 1990 and January 2000 inclusive.**

Subjects: **Patients aged 13 years and above, with non-Hodgkin's lymphomas.**

Results: **Case records were available for 207 patients, 146 males and 60 females, with one having had gender not clarified. Fifty two per cent of the patients were aged less than 40 years and 18.4% over 60 years. Forty one per cent were not properly classified histologically, seventy patients out of 190 evaluable (36.8%) had stages IVA and IVB disease at diagnosis. Twenty five out of 77(32.5%) tested positive for HIV infection, none of them being of the indolent variety. Up to 57.1% of cases of Burkitt's lymphoma tested positive for HIV infection. Cyclophosphamide, doxorubicin, vincristine and prednisone, (CHOP) chemotherapy was given to 68.7% of the patients with complete remission rates of 55.6% for those who got a minimum of six courses of chemotherapy. Only 15.3% of 105 patients evaluable were followed up for 36 months and above, the majority of patients having been lost to follow-up. Poor performance status at diagnosis correlated with shorter follow-up durations ($p<0.05$).**

Conclusion: **A good percentage of the patients were not comprehensively characterized pathologically. Standard treatment was offered to the majority of patients, and those who could afford to purchase the medicines stood good chance of achieving complete remission. Poor performance status at diagnosis correlated with shorter follow-up durations and early stage disease correlated with longer follow-up durations. Overall, the outlook for NHLs treated at KNH in the 1990s appears to have improved tremendously.**

INTRODUCTION

Non-Hodgkin's lymphomas are a complex and diverse group of neoplasms varying in natural history and patterns of response to treatment. Their classification has over the years been riddled with controversy. Many early classifications like those of Gall and Mallory, and Rappaport(1,2) were based purely on morphology while others like the Working Formulation(3) utilized primarily treatment response and survival. The Kiel, and Lukes and Collins classifications(4,5) were mainly based on cell lineage and differentiation. Because these earlier classifications have long outlived their usefulness, lymphomas are currently best classified according to the World Health Organization (WHO) update of the Revised European-American Classification of Lymphoid Neoplasms (REAL)(6,7) which is based on the principle that a classification is a list of "real" disease entities, defined by a combination of morphology, immunophenotype, genetic features and clinical features. In this classification NHLs are sub-classified into many different "real" tumour types falling under the subclasses precursor (immature) Bcell, peripheral (mature) B-cell, precursor T-cell and peripheral T-and natural killer cell origin. The most important prognostic determinant is histologic subtype, others being age, treatment, stage, sex, patients' performance status, serum LDH. Some of these factors are now put together to formulate the International Prognostic Index which in itself is a major prognostic determinant(8).

Treatment of NHLs upfront is pegged on the histologic subtype, disease stage, phenotypic expression and immunologic markers. Combination chemotherapy forms the backbone of treatment of NHLs, whether of indolent or aggressive phonetypes. For the latter there are many multidrug combinational agents but the combination of cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP) as reported by McKelvey and colleagues in the mid 1970s(9) is most favoured internationally in firstline treatment. The first step towards cure of unfavourable histology NHLs is attainment of complete remission upfront, which is the therapeutic goal. Failing cases, if chemosensitive, are managed with high dose therapy with haematopoietic stem cell rescue(10). Thirty to fifty percent of NHLs are curable with adequate therapy.

Unfortunately, because of lack of facilities for immunohistochemistry and genetic and molecular biologic techniques locally, we are so far unable to adopt the WHO update of the REAL classification. In terms of state of the art treatment we have not developed the capacity to deliver high dose chemotherapy with haematopoietic progenitor cell rescue.

We set out in a retrospective study to find out the clinicopathologic status, prognostic factors, treatment and outcome for NHLs treated at Kenyatta National Hospital in the 1990s, since the introduction of cost-sharing in public hospitals in Kenya.

MATERIALS AND METHODS

Case records of patients with non-Hodgkin's lymphomas aged 13 years and above, treated at Kenyatta National Hospital (KNH) between January 1990 and January 2000 inclusive were scrutinized. Information obtained included patients' demographic data such as sex, age at diagnosis, tribe, race, religion, area of residence; clinical and pathologic details such as histology, date of diagnosis, disease stage at diagnosis, number of sites involved, HIV status, other intercurrent illnesses, significant previous other illnesses, patients' performance status at diagnosis. Body mass index (BMI) and body surface area (BSA) were derived from weight and height. Further information included haematologic parameters, blood chemistry, treatment given upfront - if radiotherapy total number of grays, if chemotherapy - protocol and number of courses. Also checked were status of response after four courses and after six courses, date of last treatment, date of disease relapse or progression. If relapse or progression occurred - type of salvage treatment, date of salvage treatment, courses of salvage treatment, outcome of salvage treatment, last date of follow-up, date of death if recorded, causes of death if known, survival duration, follow-up duration.

Histologic classification was derived from the International Working Formulation(3) and staging was based on the Ann Arbor Classification(11), performance status was according to ECOG(12). Univariate analyses were performed with respect to age and histology, age and site at diagnosis, sites and histology, histology and HIV status, treatment upfront and histology, sites involved and HIV status.

Duration of follow-up was taken as a surrogate marker for survival and univariate analyses performed with respect to it and age, sex, histology, WBC count at diagnosis, haemoglobin level at diagnosis, performance status body mass index, status of response at four and at six courses of chemotherapy.

RESULTS

Demographic details: Records were available for a total of 207 patients, 146 males and 60 females, one had gender not stated. One hundred and seven out of 147 (51.7%) were aged less than 40 years, 61(29.5%) were aged 40-59.9 years and 38(18.4%) were aged 60 years and above. Sixty-eight out of 199(34.2%) were Kikuyus, 35(17.6%) Luos, 29(14.6%) Kambas, 23(11.6%) Luhyas, 13(6.5%) Kalenjins and 8(4.0%) were Kisiis (Table 1).

Clinical and pathologic parameters: Indolent phenotypes made up 13 out of 207 (6.3%), aggressive phenotypes 38(18.4%), highly aggressive, non-Burkitt's lymphoma 44(21.3%) and Burkitt's lymphoma 27 (13.0%). Other descriptions not well categorized were 47(22.7%) and non-Hodgkin's lymphoma not otherwise specified were 38(18.4%). Of those grouped as others, 10/47(21.3%) were classified as well differentiated, 25(53.2%) were referred to as large cell type, four (8.5%) were mycosis fungoides, five(10.6%) were anaplastic and 3(6.4%) plasmacytoid/immunoblastic. Of the 190 cases evaluable, 18(9.5%) were in stage IA, 102(53.7%) in stages IB, IIA, IIB, IIIA, IIIB; 70 (36.8%) were in stages IVA and IVB. One hundred percent of Burkitt's lymphoma cases, 54.5% of highly aggressive phenotype non-Burkitt's cases, 31.6% of aggressive phenotype cases and 30.8% of indolent phenotype cases were aged under 40 years (Table 2).

Out of 203 cases evaluable for site, 65(32.0%) had disease limited to lymph nodes, 56(27.6%) had disease in extra-nodal sites and 82 (40.4%) had disease involving both nodal and extra-nodal sites. The specific extra-nodal sites of involvement amongst 56 patients were brain and spinal cord, 13(23.2%); ear, nose, throat 14 (25%); testes/ovaries 2(3.6%); orbital 3(5.4%), others 29(51.8%) (Table 2).

Of patients aged <40 years, 41.5% had nodal disease, 61.8% had extra-nodal disease, and 53.65% had nodal and extra-nodal disease. Of patients aged >60 years, 29.2% had nodal disease 12.7% had extra-nodal disease and 14.6% had nodal and extra-nodal disease. These differences were however not statistically significant (P=0.08). Disease stage did not significantly correlate with histology (P=0.09), nor did histologic subtype correlate with performance status at diagnosis (P=0.13) (Table 3).

Tests for HIV infection were carried out in 77 out of 172 cases evaluable. For the rest no information was available. Of the 77 tested 25(32.5%) were positive and 52(67.5%) negative. Of the 25 cases who were positive

for HIV infection, none was of the indolent phenotype, while 26.7% were of aggressive phenotypes, 27.3% of highly aggressive non-Burkitt's phenotypes and 57.1% of Burkitt's types. These differences were however not statistically significant (P = 0.31). Eighteen patients out of 178 evaluable (10.1%) had ECOG performance status 0,71(39.9%) had PS 3 (Table 3).

Treatment: Eight of 173 cases evaluable (4.6%) were treated with radiotherapy upfront, 162 (93.6%) had chemotherapy and 3 (1.7%) had chemo-radiotherapy. Out of 146 cases evaluable for chemotherapy, only 66 (45.2%) received six courses and above. The rest did not get adequate treatment. Cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP) or CHOP-like chemotherapy was given to 112 out of 163 cases evaluable (68.7%), and cyclophosphamide, vincristine and prednisone (COP) to 26 (16.0%) of the cases evaluable. Thirty one out of 146 (21.2%) cases received only one course of chemotherapy. Less than 50% of the cases received at least six courses of chemotherapy. Out of 111 cases evaluable 110(99.1%) patients received standard dosing per course, one was considered under-dosed (Table 4). After four courses of chemotherapy two out of 38 cases evaluable (5.3%) achieved complete remission, 31(81.6%) partial remission, three (7.9%) stable disease and two (5.6%) progressive disease. After six courses out of 63 cases evaluable, 35(55.6%) achieved complete remission, 21 (33.3%) partial remission, three (4.8%) stable disease and four (6.3%) progressive disease. The difference in remission status at four and six courses was highly significant (P<0.001). The number of deaths recorded was 22, nine from progressive disease and five from sepsis (Table 5).

Table 1

Demographic details of patients with non-Hodgkin's lymphoma

Characteristic	No.	(%)
Sex (n = 206)		
Male	146	70.9
Female	60	29.1
Age at diagnosis (n = 206)		
< 40	107	51.9
40 - 59.9	61	29.6
≥ 60	38	18.4
Tribe/Race (n = 199)		
Kikuyu	68	34.2
Luo	35	17.6
Kamba	29	14.6
Luhya	23	11.6
Kalenjin	13	6.5
Kisii	8	4.0
Others	23	11.6

(M/F=2.43/1)

Table 2

Clinical and pathologic details of patients with non-Hodgkin's lymphoma

Characteristic	No.	(%)
Histology (n = 207)		
Indolent phenotype	13	6.3
Aggressive phenotype	38	18.4
Highly aggressive, non-Burkitt's	44	21.3
Burkitt's lymphoma	27	13.0
NHL not otherwise specified	38	18.4
Other descriptions	47	22.7
Other descriptions (n = 47)		
Well differentiated	10	21.3
Large cell type	25	53.2
Mycosis fungoides	4	8.5
Anaplastic	5	10.6
Plasmocytoid/immunoblastic	3	6.4
Disease stage at diagnosis (n = 190)		
Stage IA	18	9.5
Stage IB, IIA, IIB, IIIA, IIIB	102	53.7
Stage IVA, IVB	70	36.8
Sites of involvement (n = 203)		
Nodal	65	32
Extra-nodal	56	27.6
Nodal + extra-nodal	82	40.4
Specific extra-nodal sites (n = 56)		
Brain/spinal cord	13	23.2
Ear, nose, throat	14	25
Testes/ovaries	2	3.6
Orbital	3	5.4
Others	29	51.8
HIV status checked (n=77)		
Positive	25	32.5
Negative	52	67.5
Performance status ECOG (n=178)		
0	18	10.1
1	71	39.9
2	63	35.4
3	26	14

Table 3

Correlation of demographic, clinical and pathologic characteristics for non-Hodgkin's lymphomas

a) Sites of involvement according to age group (n = 149)

Age Group	Site: Nodal No.	(%)	Extra Nodal No.	(%)	Nodal + Extra Nodal No.	(%)
<40 (n = 105)	27	(25.7)	34	(32.4)	44	(41.9)
40-59.9 (n = 59)	19	(32.2)	14	(23.7)	26	(44.1)
≥ 60 (n = 38)	19	(50.0)	7	(18.4)	12	(31.6)
p = 0.08 - NS						

b) Disease stage against histology (n = 114)

Histology	Stage: 1A No.	(%)	IB, IIA, IIB, IIIA, IIIB No.	(%)	IVA, IVB No.	(%)
Indolent (n = 12)	0	0	8	(66.7)	4	(33.3)
Aggressive (n = 36)	3	(8.3)	20	(55.6)	13	(36.1)
Highly Aggressive (Non-Burkitt's) (n = 40)	3	(7.5)	27	(67.5)	10	(25)
Highly Aggressive (Burkitt's) (n = 26)	0	0	12	(46.2)	14	(53.8)
p = 0.09 (NS)						

c) Performance status against histology (n = 108)

Histology	Performance Status: 0 No.	(%)	1 No.	(%)	2 No.	(%)	3 No.	(%)
Indolent (n = 11)	3	(27.3)	4	(36.4)	3	(27.3)	1	(9.1)
Aggressive (n = 35)	4	(11.4)	16	(45.7)	10	(28.6)	5	(14.3)
Highly aggressive (non-Burkitt's) (n =38)	5	(13.2)	13	(34.2)	18	(47.4)	2	(5.3)
Highly aggressive (Burkitt's) (n = 24)	0	0	12	(50)	5	(20.8)	7	(29.2)
p = 0.13 (NS)								

d) HIV status against histology (n = 108)

Histology	HIV Status: Positive No.	(%)	Negative No.	(%)
Indolent (n = 4)	0	(0)	4	(100)
Aggressive (n = 15)	4	(26.7)	11	(73.3)
Highly aggressive (non-Burkitt's) (n =22)	6	(27.3)	16	(72.7)
Highly aggressive (Burkitt's) (n= 7)	4	(57.1)	3	(42.9)
Not Specified (n = 29)	11	(37.9)	18	(62.1)
p= 0.31 (NS)				

Table 4

Treatment

Characteristic	No.	(%)
Treatment upfront (n = 173)		
Radiotherapy	8	4.6
Chemotherapy	162	93.6
Chemoradiotherapy	3	1.7
Types of chemotherapy (n = 163)		
CHOP/CHOP-like	112	68.7
COP	26	16
ChlP	9	5.5
MACOP-B	2	1.2
Other	14	8.6
Dosing of chemotherapy (n = 111)		
Standard	110	99.1
Underdosed	1	0.9
Overdosed	0	0

Table 5

Outcome of treatment

	Status of response							
	CR		PR		SD		PD	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
After 4 Courses (n = 38)	2	(5.3)	3	(81.6)	3	(7.9)	2	(5.3)
After 6 courses (n = 63)	35	(55.6)	21	(33.3)	3	(4.8)	3	(6.3)

Table 6

Clinico-pathologic factors in relation to follow-up of NHL (months)

Characteristic	No.						(%)	
	Status of remission after six courses against follow-up (n=30)							
Status of remission	<12		12-35.9		36-59.9		≥60	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
CR (n = 20)	3	(15)	10	(50)	2	(10)	5	(25)
PR (n = 5)	1	(20)	1	(20)	0	(0)	3	(60)
SD (n = 2)	0	(0)	2	(100)	0	(0)	0	(0)
PD (n = 3)	3	(100)	0	(0)	0	(0)	0	(0)

CR = complete remission, PR = partial remission, SD = stable disease, PD = progressive disease

P>0.05 (NS)
Follow-up against sex (n = 104)

	Follow-up (months)							
Sex	<12		12-35.9		36-59.9		≥60	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Male (n = 72)	43	(59.7)	17	(23.6)	4	(5.6)	8	(11.1)
Female (n = 34)	18	(52.9)	10	(29.4)	3	(8.8)	3	(8.8)

P> 0.5 (NS)

Follow-up at ≥ 36 months against performance status (87 cases evaluable for follow-up)

	No.	(%)
PS0 (n = 13)	3	23.1
PSI (n = 21)	9	20.5
PS2 (n = 44)	3	14.3
PS3 (n = 21)	0	0

p = 0.9 (NS)

p < 0.05 (S) for this subgroup but for total duration of follow up, p = 0.9

Follow-up at ≥ 36 months against wbc count (97 cases evaluable for follow up)

	No.	(%)
< 4 x 10^9/litre (n = 13)	2	15.4
4 -10 x 10^9/litre (n = 59)	9	15.3
>10 x 10^9 litre (n = 25)	4	16

p = 0.9 (NS)

Follow-up for ≥ 36 months against Hb (97 cases evaluable for follow-up)

	No.	(%)
< 10g/dl (n =21)	2	9.5
≥ 10g/dl (n =76)	13	17.1

PS= 0.2 (NS)

PS= Perfomance Status, NS = Not Significant

Follow-up according to disease stage at diagnosis (n = 98)

Stage	Follow-up (months) <12		12-35.9		36-59.5		≥60	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
AI, IIA (n=13)	3	(23.1)	5	(38.5)	3	(23.1)	2	(15.4)
IB, IIB, IIIA (n=49)	34	(69.4)	10	(20.4)	1	(2.0)	4	(11.8)
IIB, IV(n=36)	19	(52.8)	11	(30.6)	1	(10.5)	5	(13.9)

X^2 = 9.31 ; P = 0.021

Out of 105 cases evaluable, 15.3% were followed up for 36 months and above, 10.5% for 60 months and above. White blood cell counts at diagnosis of <4 x 10^9 litre, 4 -10 x 10^9/litre and >10 x 10^9 litre did not correlate with follow-up duration (P = 0.9). Ninety seven cases were evaluable for follow-up against haemoglobin level at diagnosis. Of those with haemoglobin < 10g/dl, 9.5% were followed up for 36 months and above while 17.1% of those with haemoglobin of 10g/dl and above were followed up for 36 months and above. These differences were not statistically significant (P = 0.2) (Table 6).

Twenty five cases had BMI checked against remission status after six courses. Ten out of eighteen (55.6%) with BMI <22.8 had CR as compared with only 2/7 (28.6%) with BMI ≥22.8, but again the numbers were small and the differences were not statistically significant (P=0.6). Thirty cases were evaluable for status of remission after six courses against follow-up. Thirty five percent of 20 patients who had CR after six courses were followed up for ≥36 months. Three out of five of those with PR at six courses were followed up for ≥36 months. None of those who had stable and progressive disease were followed up for ≥36 months. The numbers were small and these differences were not significant (P = 0.05). One hundred and four cases were analyzed for sex against follow-up and there was no significant difference (P = 0.05). Out of 87 cases evaluable for performance status against follow-up, no patients with PS of 3 were followed up for ≥36 months, and none with performance status of 0 were followed up for less than a month, which was statistically significant (P<0.05), but total duration of follow-up did not correlate with performance status (p=0.9).

Disease stage at diagnosis on the other hand correlated with follow-up. Of the 98 cases evaluable

patients diagnosed with early stage disease were followed up for longer duration than those diagnosed with advanced disease (Table 6).

DISCUSSION

Non-Hodgkin's Iymphomas are diverse types of Iymphoid neoplasms lumped together under one entity. On the whole they affect more males than females and the ratio described in this study of 2.5:1 tallies with what is established(13,14). Specific histologic subtypes tend to cluster around certain age groups, like follicular Iymphoma and small Iymphocyte Iymphoma in the middle aged to elderly, Burkitt's Iymphoma and precursor B/T cell Iymphoblastic Iymphoma/leukaemia in the younger population. With more than 20 different subtypes the age scatter seen in this series with 52% being less than 40 years and 18% above 60 years is expected. Globally there are certain racial variations among NHL patients, with follicular Iymphoma being more common amongst the European and North-American Caucasians while T-cell types tend to feature more amongst the Oriental races. Not much is known about the distribution amongst the Negroid tribes of Africa except for endemic Burkitt's Iymphoma along the Iymphoma belt. The high frequency of occurrence amongst the Kikuyu tribe at 34% followed by the Luos who make up half of that then Kambas and Luhyas would at best reflect the strong representation of these ethnic groups in and around Nairobi, and probably strong referral systems obtaining in various provincial hospitals in areas populated by these tribes.

Some of the patients in this series had their diagnosis made at the time when the International Working Formulation was the most favoured Iymphoma classification system globally(3). Others were diagnosed after the adoption of the Revised European American Lymphoma (REAL) classification published by Harris and colleagues in 1994 and its World Health Organization (WHO) update published in 1997 (6,7). Unfortunately, the need for application of immunohistochemistry has made it difficult to apply the new Iymphoma classification not only in developing countries but also in community practices in developed countries. Most of the cases in our series were classified using diverse methods ranging from the Rappaport system which became obsolete in the early 1980s to the Working Formulation which became defunct in mid to late 1990s. An attempt was made retrospectively to apply the Working Formulation nomenclature which would have been the simplest to apply, but this still left out 30% of the cases not histologically characterized. Since histologic subgroups of NHLs carry vast prognostic implications, we were dealt our first blow in an attempt to identify locally, easy prognostic determinants. Burkitt's Iymphoma made up 22.1% of the cases. With a median age of occurrence of this condition at seven years in Kenya (Othieno-Abinya and Nyong'o, unpublished data), and with its high prevalence, inclusion of paediatric cases would have pushed up the percentage of those below 40 years tremendously. Aggressive and highly aggressive types were seen predominantly in younger patients, and this is expected.

The distribution of nodal and extra-nodal disease was fairly similar, and this was interesting. Nodal disease occurs more frequently than extra-nodal disease, but since aggressive Iymphoma types which were predominant in this series tend to be extra-nodal, this finding is not surprising. The prevalence of positive serology for human immunodeficiency virus (HIV) infection was 32.5% of those tested. The HIV seroprevalence rate for Kenya is about 7% (15). It can be argued that there was bias towards testing those who were suspected to be infected. However it is our policy that all NHL cases are tested for HIV infection upfront. It is instructive to note that none of the indolent Iymphoma types tested positive while the highly aggressive types, Burkitt's in particular had high frequencies of HIV seroprevalence. The question is, whether all these cases were BL or some were diffuse large B cell Iymphomas? Subgroup analysis was not carried out to correlate HIV infection with nodal or extra-nodal disease because of small numbers. Since Burkitt's Iymphoma is predominantly extra-nodal and a significant percentage of the patients were HIV infected, this could have increased the number of cases with predominantly extra-nodal disease. The presence of extra-nodal disease pushes disease stage higher for the different histologic subtypes. This did not come out clearly because a good number of cases were not properly characterized histologically and in retrospective studies, stage designations are commonly flawed.

About 50% of the patients analysed had ECOG PS 2 (12) again, reflecting the reasonably good general condition of patients with NHLs at diagnosis. One should not forget that patients with PS >3 are unlikely to have been successfully referred to KNH.

The combination of cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP) that was originally reported by McKelvey and colleagues in 1976 (9) is the standard of care for adults with aggressive phenotype NHLs (16). Attempts to modify the administration to make it more effective by either increasing dose density at three week intervals or by continuous infusion which do not appear to make any impact, or by increasing the dose intensity by giving it at two weeks intervals which appears to improve the long term outcome, have been made(17-19). CHOP or CHOP-like protocol was used in 68.7% of the cases evaluable. The standard dosing per course was considered adequate in virtually all patients but the relative dose-intensity was not calculated. Unfortunately, the treatment was not sustained and <50% of the cases received six courses and above. The recommended number of courses is six to eight, depending on the stage at which complete remission is achieved after which a further

two consolidating courses are given. Achievement of complete remission with front-line chemotherapy is the first step towards cure of any chemocurable neoplasm and adequacy of treatment determines this. After four courses, only 5.3% of the patients evaluable achieved complete remission and the number shot up to 55.6% after six courses for those who had adequate treatment. These differences were highly significant ($p<0.001$). It is instructive to note that compared with historical controls(13), the outcome for these patients in this institution appears to have improved. The problem was that less than 50% of the patients could afford to go through the intended course of chemotherapy, mainly because of cost.

Whereas the treatment for disseminated indolent phenotype NHLs, especially of B-cell origin such as follicular lymphoma and small lymphocyte lymphoma is still generally palliative, the use of purine analogs especially fludarabine in combination with an alkylating agent such as cyclophosphamide may alter the outcome (20). Addition of anti-CD 20 monoclonal antibody (rituximab) improves progression-free survivals (21). High-dose chemotherapy with haematopoietic progenitor cell rescue followed by rituximab for minimal residual disease is another promising approach (22). A small number (6.3%) of the lymphomas in our series were of indolent phenotype and 5.5% were treated with chlorambucil and prednisone which would ordinarily be used for such cases, and a combination of cyclophosphamide, vincristine and prednisone (COP) was used in 16% of the cases. Today, addition of rituximab to CHOP (R-CHOP) is also promising in aggressive phenotype B-cell lymphomas (23-25). The majority of our patients were lost to follow-up, only 10.5% of the patients were followed up for ≥60 months, and only 15% for ≥36 months.

Federico and colleagues found gender, B-symptoms, number of extra-nodal sites, serum LDH and elevated ESR as key features, for prognosis of follicular lymphoma irrespective of grade(26). Whereas subgroup analysis was not carried out for various histologic subtypes which was impossible in our series, gender did not correlate with follow-up. Serum LDH was not routinely tested, and neither was ESR. The rest did not correlate with follow-up. In a population based series, Maartense and colleagues had identified amongst others, performance status and age >70 years as the main prognostic factors for follicular lymphoma patients(27), whereas elevated LDH and stages III and IV disease were more important as prognostic factors in patients with diffuse large-B-cell lymphoma. Stage correlated with follow-up duration amongst our patients. None of our patients with ECOG PS3 were followed up for >36 months and none with PS0 were followed up for <1 month, but these differences were not significant ($P = 0.9$). This could highlight haphazard follow-up and the error of trying to derive patients' performance status in retrospective studies.

Haemoglobin level at diagnosis and white blood cell counts did not correlate with follow-up, but this is not surprising as they are not established as prognostic factors. It is tempting to speculate that circulating lymphoid cells in lymphoma would signify leukaemic phase hence poor prognosis, and that a low haemoglobin level would signify among others, bone marrow infiltration hence poor prognosis, but this happens not to be the case because several other variables are in play.

Early disease stage at diagnosis significantly correlated with longer durations of follow-up in this study. This, despite serious limitations in follow-up could still confirm the prognostic value of disease stage in NHL, though to a limited extent.

CONCLUSION

A good percentage of our NHL patients were not comprehensively classified pathologically, and a good percentage of the highly aggressive phenotypes were likely to test positive for HIV infection. Standard treatment was offered to the majority of the patients but a good number could not afford to complete the treatment because of the cost of drugs. Those who completed treatment had a 57% chance of achieving complete remission which compares well with results elsewhere. Losses to follow-up were high, further making it difficult to test various prognostic variables. Early disease patients were more likely to be followed up for longer durations and on the whole, the outlook for NHLs treated at KNH in the 1990s appears to have improved tremendously, but cost is still a major impediment for adequate delivery of treatment.

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