

# Challenges in the Pharmacological Management of Non Hodgkin's Lymphoma in Children in the Maintenance Phase of Therapy at Kenyatta National Hospital

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## Abstract

**Background:** Non Hodgkin's lymphoma is an extremely chemo sensitive with a five year event free survival of greater than 90% in developed countries and a one year survival rate of 40-50% in developing countries. There have been no documented studies done at Kenyatta National Hospital on the various challenges faced by patients and their guardians that may hinder its optimal management.

**Objectives:** To investigate the major challenges faced in the management of Non Hodgkin's lymphoma in pediatric patients in the maintenance phase.

**Methodology:** This was a hospital based cross-sectional study, among 19 Paediatric outpatients with Non Hodgkin's Lymphoma and in the maintenance phase of therapy at Kenyatta National Hospital. Data was collected using structured questionnaires and from patient files and was analyzed using Statistical Package for Social Sciences version 17.0. P values  $\leq 0.05$  were considered significant. Fischer's exact test was used to test for association between adherence and various categorical variables such as patient factors, guardian factors and hospital and service delivery setup.

**Results:** Of the 19 patients, 13 (68.4%) were found to be male. The mean age for all the patients was 9.84 years (95% CI: 8.3, 11.3). 42.1% of the patients had missed their oral medication. The method of acquisition of oral medication, estimated expenditure on medication per month and whether the guardian was counseled on the side effects of the medication, were found to be statistically significant (p value 0.037, 0.02 and 0.037 respectively). The most prevalent (94.7%) side effects were loss of hair followed by change in nail/skin pigmentation (73.7%) with the least observed side effects being dizziness, constipation and tingling sensation of lower extremities. Cumulative doses of doxorubicin used showed that majority of the patients (63.1%) had cumulative doses between 200-400mg/m<sup>2</sup> while only 10% had cumulative doses above 400mg/m<sup>2</sup>.

**Conclusion:** The overall adherence to oral chemotherapy was found to be 57.9%. Method of acquisition of the oral medication, estimated expenditure on medication per month and counseling on medication and its side effects were significant barriers to adherence. Based on cumulative doses of doxorubicin used, 63.1% of the patients in this study stand a low risk of developing cardio toxicity with only 10% standing a significant risk of cardio toxicity.

**Keywords:** Non Hodgkin's Lymphoma; Oral Chemotherapy; Adherence; Side Effects; Cumulative Doses

## Introduction

Non Hodgkin's lymphoma (NHL) is a group of related malignancies of the lymphatic system [1]. Some of the Non Hodgkin's lymphoma are among the most rapid growing and aggressive of all cancers while others are indolent.

There are three main types of Non Hodgkin's lymphoma in children and they include lymphoblastic lymphoma, small non cleaved cell lymphoma and large cell lymphoma all of which 90% of the time have been classified as high grade disease compared to adults [1].

Small non cleaved cell lymphoma (Burkitt's lymphoma) represents over half of childhood cancers in equatorial Africa and in Kenya a study done by Cool, *et al.* showed that majority of the NHL cases were of the B cell lineage with Burkitt's lymphoma being the most common followed by diffuse large B cell lymphoma [2]. Burkitt's lymphoma has been shown to be mainly a childhood tumor and accounts for up to 36% of childhood cancers and 70% of childhood lymphomas in sub-Saharan Africa [3].

It has been proven that most types of Non Hodgkin's lymphoma in particular Burkitt's lymphoma are curable with long term survival rates [4]. However, various factors in most developing countries have made this unachievable for example cost of medication and services offered in the management of Burkitt's lymphoma which varies from 450 US dollars to 2800 US dollars whereas income of the majority of the population in most developing countries is less than 1 US dollar per day [5,6]. The education level of the caregivers, side effects of the medication, social and cultural factors as well as counseling of caregivers have also been shown to hinder optimal management of Non Hodgkin's lymphoma [7]. So far there have been no documented studies done in KNH on the various challenges faced by patients and guardians during the management of Non Hodgkin's lymphoma and any other factors that may hinder its optimal management.

Therefore the objective of this study was to investigate the major challenges faced in the management of Non Hodgkin's lymphoma in pediatric patients in the maintenance phase. This was done by investigating the factors that affect adherence to oral chemotherapy, prevalence of side effects, assessing the guardians knowledge on the disease and its management and determination of patients with appropriate drug use and cumulative doses of doxorubicin used.

## Methodology

### Study design

The study conducted was a hospital based cross-sectional study

### Study area

This study was carried out at the Kenyatta National Hospital (KNH) pediatric haematology outpatient clinic 23 between 19<sup>th</sup> July, 2013 and 28<sup>th</sup> October 2013. KNH is the largest teaching and referral hospital in east and central Africa and serves as the main referral for most pediatric cancer patients in the country.

### Target population

Pediatric patients attending the pediatric outpatient clinic that had been diagnosed with Non Hodgkin's lymphoma and were in the maintenance phase of therapy [8].

### Inclusion and Exclusion criteria

The patients that were included in the study were pediatric patients being managed for Non Hodgkin's lymphoma in the maintenance phase of therapy and were using 6Mercaptopurine, Methotrexate, Vincristine, Adriamycin and Cyclophosphamide.

Patients who were on any other drug regimens, were below two years of age and had any other co-morbidities were excluded from the study.

### Sample size determination and sampling procedure

The sample size was calculated using the Fischer's formula. The desired sample size was 37 patients. The patients were first identified by going through the patient files delivered at the clinic and selecting those that met the inclusion criteria. A final study sample of 19 patients was used.

### Data collection

Data was collected by filling in the questionnaire by the principal investigator by holding face to face interviews with the guardians to the patients after informed consent. The guardians were interviewed to determine adherence to oral chemotherapy, knowledge on the disease, medication and its side effects and appropriate drug use. The files to the same patients were perused for side effects due to medication, confirmation on appropriate drug use for parenteral medication and cumulative doses of doxorubicin used.

Adherence was measured by determining number of prescribed oral chemotherapy taken in the last two weeks.

## Quality Assurance

### Pilot Study

A pilot study was done by randomly selecting 5 study subjects. The shortcomings were detected and were used to improve the data collection instrument.

### Validity

Internal validity was ensured by using simplified language in the questions asked which were geared towards the study objectives. Adherence was further validated by using a two week recall period as opposed to one month to avoid recall bias.

## Ethical Considerations

Approval to carry out the study was obtained from the Kenyatta National Hospital/ University of Nairobi Ethics and Research Committee (KNH/UON ERC). Approval was granted as per letter of reference Number KNH-ERC/A/190 dated 5<sup>th</sup> July 2013. Patients' names did not appear on the data collection forms and instead serial numbers were used. The data collection materials were kept under lock and key during the entire study time.

## Data Analysis

Data was analyzed using SPSS version 17.0. Numerical data was summarized as means. Mann-Whitney test was used to test for difference in medians values for the continuous variables among those children who were adhering to oral treatment against those who were not adhering. Additionally their mean values were computed with the accompanying 95% confidence intervals. Categorical data was summarized in percentages and graph form. To test for association between adherence and various categorical variables Fisher's exact test was used. Variables were cross tabulated to assess factors that contribute to adherence to oral medication. P-values of less than 0.05 were considered significant.

## Results

### Baseline characteristics of the patients

The baseline characteristic of the 19 patients is shown in Table 1. Most (68.4%) of the patients were male (n=13). The mean age of the patients was 9.84 years with a minimum of 4 years and a maximum of 13 years.

Variable	Frequency (N=19)	%
<b>Sex</b>		
Female	6	31.6
Male	13	68.4
<b>BMI</b>		
Ideal	14	73.7%
Underweight	3	15.8%
Overweight	2	10.5%
<b>AGE</b>		
Mean	9.82 (95% CI:8.3, 11.3)	
Minimum	4	
Maximum	13	

Table 1: Patient baseline characteristics

### Characteristics of the guardians

Most (84.2%) of the guardians to the patients were married with majority being unemployed. Majority of the spouses to the guardians were self employed at 50%. The average monthly income was found to be between Ksh 0-9,999 (US \$0-99).

31.6% of the guardians had primary school education while the majority (47.4%) had secondary school education a small number of patients had tertiary education or no education at all. This is as shown in Table 2.

Variable	Frequency (N=19)	%
<b>Marital status</b>		
Single	3	15.8
Married	16	84.2
<b>Employment status</b>		
Employed	0	0
Self Employed	7	36.8
Unemployed	12	63.2
<b>Spouse employment status (n=16)</b>		
Employed	6	37.5
Self Employed	8	50.0
Unemployed	2	12.5

Variable	Frequency (N=19)	%
<b>Average Monthly income</b>		
0-9,999	13	68.4
10,000-29,999	4	21.1
30,000-49,999	2	10.5
<b>Education Level</b>		
Primary	6	31.6
Secondary	9	47.4
Tertiary	2	10.5
Others	2	10.5

Table 2: Information on the guardian

## Knowledge assessment

Most of the guardians claimed on knowing what their children were being managed for and the response on the explanations they gave were graded as either:

Not informed - if they gave the wrong information or no information on the disease

Fairly informed- if they gave correct but limited information on the disease

Well informed- If they gave correct and comprehensive information on the disease

The major source of information for the guardians on the disease was from a health care provider with 52.6% being fairly informed and approximately 20% being well informed or not informed.

Majority of the patients had never had any counselling on side effects of the medication with only 42.1% being counselled on side effects most (62,5%) of which was done by a nurse.

Loss of hair, vomiting and changes in skin or nail pigmentation were considered as side effects of medication by most of the guardians while none of them considered constipation as a side effect as shown in Table 3.

Variable	Frequency	%
<b>Knows what your child is being treated for</b>		
Yes	18	94.7
No	1	5.3
<b>Explanation on what the child is being treated for</b>		
Not informed	4	21.1
Fairly informed	10	52.6
Well informed	5	26.3
<b>Information source (n=18)</b>		
Health provider	18	100%
<b>Aware of the medication your child is taking</b>		
Yes	17	89.5
No	2	10.5
<b>Correct knowledge on medicine duration</b>		
Yes	17	89.5
No	2	10.5
<b>counseled on side effects of the medication</b>		
Yes	8	42.1
No	11	57.9
<b>Counseled by whom</b>		
Clinician	3	37.5
Nurse	5	62.5
<b>Proportions that considers the following as possible side effects of the drugs</b>		
Vomiting	17	89.5

Variable	Frequency	%
<b>Proportions that considers the following as possible side effects of the drugs</b>		
Diarrhea	3	15.8
Lack of appetite	8	42.1
Constipation	0	0
Loss of hair	18	94.7
Darkening of the skin	13	68.4
Signs of Myelosuppression	5	26.3

Table 3: Knowledge assessment

## Factors affecting adherence

Adherence to oral chemotherapy was determined using self report from the patients' guardians. Adherence was taken to mean having taken all prescribed oral chemotherapy in the last two weeks while non adherence was taken to mean having missed any doses of oral chemotherapy in the last two weeks.

42.1% (n=8) of the patients had missed their oral medication in the last two weeks with a majority (50%) having missed because the guardians could not afford to buy the medication followed by those who could not find the drug (25%).

Acquisition of oral medication for most of the patients (57.9%) was by buying using their own cash. The estimated expenditure per month for the oral medication was found to be between ksh 6,500 (US \$65) and ksh 25,000 (US 250) with a mean of ksh 11,321 (US \$113.21 ) (Table 4).

Variable	Frequency	%
<b>Medication source-Injectable</b>		
Hospital pharmacy	19	100
<b>Medication source-orals</b>		
Hospital pharmacy	5	26.3
Private pharmacy	14	73.7
<b>How they acquire orals medications</b>		
Buys cash	11	57.9
Buys cash with some of it donated	3	15.8
Pay by insurance	4	21.1
Pays by insurance and some are cash donated	1	5.3
<b>How they find cost of the medicines</b>		
Easily affordable	1	5.3
Fairly affordable	2	10.5
Expensive	10	52.6
Unaffordable	6	31.6
<b>Estimated expenditure on medication per month</b>		
Mean	11,321.43 (95% CI 8, 233.6, 14, 409.2)	
Minimum	6,500	
Maximum	25,000	
<b>Child has missed any of their oral medication in the last 2 weeks</b>		
Yes	8	42.1
No	11	57.9
<b>Why the child missed drugs (n=8)</b>		
Child got worse on taking the medication	1	12.5

Variable	Frequency	%
<b>Why the child missed drugs (n=8)</b>		
Could not afford to buy the medication	4	50.0
Forgot	1	12.5
Others (e.g. could not find drug)	2	25.0
<b>Number that missed each drug (n=8)</b>		
Oral methotrexate	6	75.0
Oral 6-Mercaptopurine	8	100.0
<b>Number of doses missed Oral methotrexate (n=6)</b>		
1 dose	3	50.0
2 doses	3	50.0
<b>Oral 6-mercaptopurine (n=8)</b>		
1-7 doses	3	37.5
8-14 doses	5	62.5
<b>Other form of medication given to the child to manage for the disease</b>		
Yes	2	10.5
no	17	89.5
<b>Other medication given (n=2)</b>		
Folic	1	50
Wheat grass	1	50

Table 4: Factors affecting adherence

### Relationship between adherence to oral chemotherapy and baseline characteristics of the patients

Various patient variables were cross tabulated with adherence to oral medication using the Fisher's exact test to assess whether there was significant association. There was no significant association between the baseline characteristics and adherence to oral chemotherapy ( $P>0.05$ ). However adherence to oral chemotherapy was more in children over ten years of age (70%) compared to those less than ten years (44.4%), (Table 5).

Variable	Adherent to Oral treatment		Total	P-value
	No	Yes		
<b>Sex of the child</b>				
Female	3 (50.0%)	3 (50.0%)	3 (50.0%)	0.506
Male	5 (38.5%)	8 (61.5%)	8 (61.5%)	
<b>BMI categories</b>				
Ideal	6 (42.9%)	6 (42.9%)	14 (100.0%)	0.664
Over/ under	2 (40.0%)	2 (40.0%)	5 (100.0%)	
<b>Child's age</b>				
<10	5 (55.6%)	4 (44.4%)	9 (100.0%)	0.255
>=10	3 (30.0%)	7 (70.0%)	10 (100.0%)	

Table 5: Cross tabulation of adherence with patient baseline characteristics

### Relationship between adherence and guardian related factors

The method of acquisition of oral medication, estimated expenditure on medication per month and whether the guardian was counseled on side effects of the medication were found to significantly correlate with adherence (P value 0.037, 0.02 and 0.037 respectively). This is as shown in Table 6.

Variable	Adherent to Oral treatment		Total	P-value
	No	Yes		
<b>Marital status</b>				
<b>Single</b>	2 (66.7%)	1 (33.3%)	1 (33.3%)	0.376
<b>Married</b>	6 (37.5%)	10 (62.5%)	10 (62.5%)	
<b>Occupation</b>				
<b>Self Employed</b>	Self Employed	4 (57.1%)	7 (100.0%)	0.663
<b>Unemployed</b>	Unemployed	7 (58.3%)	12 (100.0%)	
<b>Average Monthly income</b>				
<b>0-9,999</b>	6 (46.2%)	7 (53.8%)	13 (100.0%)	0.494
<b>Above 10,000</b>	2 (33.3%)	4 (66.7%)	6 (100.0%)	
<b>Education Level</b>				
<b>Primary and below</b>	3 (37.5%)	5 (62.5%)	5 (62.5%)	0.551
<b>Secondary and above</b>	6 (46.2%)	7 (53.8%)	7 (53.8%)	
<b>Counseled on side effects of the medication</b>				
<b>yes</b>	1 (12.5%)	7 (87.5%)	8 (100.0%)	0.037
<b>no</b>	7 (63.6%)	4 (36.4%)	11 (100.0%)	
<b>Counseled by whom</b>				
<b>Clinician</b>	1 (33.3%)	2 (66.7%)	3 (100.0%)	0.375
<b>Nurse</b>	0 (0.0%)	5(100.0%)	5 (100.0%)	
<b>Medication source-orals</b>				
<b>Hospital pharmacy</b>	1 (20.0%)	4 (80.0%)	5 (100.0%)	0.267
<b>Private pharmacy</b>	7 (50.0%)	7 (50.0%)	14 (100.0%)	
<b>How they acquire orals medications</b>				
<b>Buys using own cash</b>	7 (63.6%)	4 (36.4%)	11 (100.0%)	0.037
<b>Others</b>	1 (12.5%)	7 (87.5%)	8 (100.0%)	
<b>How they find cost of the medicines</b>				
<b>Affordable</b>	Affordable	8 (61.5%)	13 (100.0%)	0.506
<b>Unaffordable</b>	Unaffordable	3 (50.0%)	6 (100.0%)	
<b>Estimated expenditure on medication per month</b>				
<b>&lt;10,000</b>	0 (0%)	6 (100.0%)	6 (100.0%)	0.02
<b>≥10,000</b>	7 (87.5%)	1 (12.5%)	8 (100.0%)	

NB significant P values are in bold

**Table 6:** Cross tabulation of adherence with guardian related factors

## Prevalence of side effects

The major (94.7%) side effect experienced by patients was loss of hair followed by a change in skin/nail pigmentation (73.7%). Myelosuppression was also observed with 21.1% having anaemia and 15.8% having neutropenia. The least observed side effects were dizziness, constipation and tingling sensation of the lower extremities as shown in Table 7.

Side effect	Frequency (N=19)	Proportions (%)
<b>Vomiting</b>	12	63.2
<b>Diarrhoea</b>	2	10.5
<b>Hyperacidity/ stomach ulcers</b>	1	5.3
<b>Mouth ulcers</b>	6	31.6
<b>Tingling sensation or pain in the lower extremities</b>	1	5.3

Side effect	Frequency (N=19)	Proportions (%)
Dizziness	0	0
Constipation	0	0
Loss of hair	18	94.7
Change in skin/nail pigmentation	14	73.7
Anaemia	4	21.1
Neutropenia	3	15.8
Thrombocytopenia	0	0.0

Table 7: Prevalence of side effects

### Proportion with appropriate drug use

It was observed that most of the patients received their parenteral medication at the right dose (89.5-100%) and right frequency (100%). As for the oral medication, 63.2% of the patients received the right dose of 6-Mercaptopurine while majority (68.4%) of the patients received an under dose of oral methotrexate (Table 8).

Drug name	Right Dose	Under dose	Over dose	Right Frequency
6-Mercaptopurine	12 (63.2%)	7 (36.8)	0 (0.0%)	18 (94.7%)
Oral Methotrexate	5 (26.3%)	13 (68.4%)	1 (5.3%)	19 (100%)
Intrathecal Methotrexate	19 (100%)	0 (0.0%)	0 (0.0%)	19 (100%)
Vincristine	18 (94.7%)	1 (5.3%)	0 (0.0%)	19 (100%)
Doxorubicin	17 (89.5%)	1 (5.3%)	1 (5.3%)	19 (100%)
Cyclophosphamide	15 (78.9%)	1 (5.3%)	3 (15.8%)	19 (100%)

Table 8: Proportion with appropriate drug use

### Cumulative doses of doxorubicin used

It was observed that majority (83.3%) of the female patients had cumulative doses of doxorubicin of less than 200mg/m<sup>2</sup>, of which most of them were below twelve years of age. In male patients, majority (80%) of them had cumulative doses of doxorubicin between 200-400mg/m<sup>2</sup> with most of them being below twelve years (Table 9).

	Cumulative doses for doxorubicin			Totals
	<200mg/m <sup>2</sup>	200-400mg/m <sup>2</sup>	>400mg/m <sup>2</sup>	
<b>Females</b>				
≤12 years	5 (83.3%)	1 (16.7%)	0 (0.0%)	6 (100.0%)
>12 years	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
<b>Males</b>				
≤12 years	1 (10.0%)	8 (80.0%)	1 (10.0%)	10 (100.0%)
>12 years	0 (0.0%)	3 (100.0%)	0 (0.0%)	3 (100.0%)

Table 9: Cumulative doses of doxorubicin

## Discussion

A total of nineteen patients were included in the study of which most of (68.4%) the patients were male at (n=13). This is similar to most studies done in Kenya by Mwanda, *et al.* and similar studies done in Uganda and Malawi which showed males being more susceptible to the disease than females [9-11].

The mean age of the patients in this study was 9.82 years (95% CI: 8.3, 11.3) with a minimum age of 4 years and a maximum age of 13 years. In Malawi the peak age was found to be 7.2 years with a range of 4-14 years [11].

A majority of the guardians to the patients had a monthly income of Ksh 0- 9,999 which is similar to most caregivers in other developing countries whereby studies done showed that most of the population earned less than 1 US dollar per day [5].

In this study 42.1% of the patients were found to be non adherent to their oral medication. In a similar study done there was non compliance to oral 6- mercaptopurine of 33.3% in children with leukemia detected through interviews and a total of 50.3% non compliance when all other methods of detecting non compliance were included. Another study also showed non adherence in children with cancer at 33% using laboratory assays of the drugs as a method of detecting non adherence [12,13].

No statistical association was observed between age and adherence in this study which is similar to a study done where there was no association between age and non-adherence [13]. However a study done by Oliveira, *et al.* showed age as having an association with non adherence whereby non adherence was more in adolescents than in younger children [12].

The average monthly income earned by the guardians was shown to have no significant association with adherence in this study. These findings were consistent with similar studies which concluded that there was no statistically significant association between non compliance and low per capita family income [11,12]. The level of education and knowledge of the disease of the guardians were also shown to have no statistical significance in relation to adherence which is similar to some studies where demographic factors such as level of education, knowledge of the disease and race were found to have no association with adherence [14]. The lack of statistical association between the various patient characteristics and adherence can be further attributed to the fact that for pediatric patients, adherence is highly dependent on the caregivers of the children. This is shown in various studies where there was better adherence found in the older population excluding the very elderly than in the younger population [15].

Counseling on the side effects of the medication was found to have significant statistical association with adherence (P value 0.037). Other studies have shown that non adherers had a less well developed understanding of their illness in terms of prognosis and a less perceived vulnerability especially in the maintenance phase where the patients were asymptomatic. This has been attributed to poor patient counseling and poor doctor to patient communication [16].

How the patients acquire their oral medication was also found to be statistically significant (P value 0.037). A study done in eleven countries showed marked effects of insurance coverage on adherence whereby very few (8.5%) were non adherent to their medication due inability to afford treatment since most of them had an insurance cover [17].

The estimated expenditure on medication per month was found to have a significant relationship with adherence in this study (P value 0.02) whereby the minimum amount spent on medication was found to be ksh 6,500 (US \$65) with a maximum of Ksh 25,000 ( US \$250). Other studies done in most developing countries such as Ivory Coast, Malawi and Nigeria showed that the cost of medication and services offered in management of Burkitt's lymphoma ranged from 450 US dollars to 2800 US dollars and since most of the patients were unable to pay for the treatment it led to treatment abdication [6,18].

A majority of the guardians were found to be fairly informed on the disease with the major source of information being from a health care provider. A large number were also aware of the medication the child was taking and duration of treatment in the maintenance phase. However a similar study done in Zambia showed less than 50% of the caregivers understood the nature of the child's leukemia [19]. This difference can be attributed to the fact that the patients in this study were in the last phase of treatment and therefore the caregivers had a longer time to acquire the information on the disease and its management unlike in the study done in Zambia.

A large number of the patients considered loss of hair as a possible side effect of the medication used followed by vomiting, changes in nail or skin pigmentation and fatigue. A study done in Australia on patient perception of the side effects of cancer chemotherapy also found vomiting, loss of hair and tiredness as the major physical side effects of medication [20].

In this study the most prevalent side effect experienced by the patients was loss of hair (94.7%), followed by a change in skin/nail pigmentation (73.7%), vomiting (63.2%), mouth ulcers (31.6%) and myelosuppression with anaemia being most common (21.1%). The least observed side effects were dizziness, constipation and tingling sensation of the lower extremities. In a study done by Sitzia, *et al.* the most common side effects observed using CHOP in management of Non Hodgkin's lymphoma were alopecia with all patients having experienced some hair loss, fatigue was the second most common side effect, followed by nausea, constipation and difficulty in sleeping [21].

In other studies done myelosuppression was also found to be the most prevalent side effect followed by mucositis, vomiting and diarrhea [22,23]. However in this study, myelosuppression is not as prevalent as in most other studies since in this study focus was on the maintenance phase where the doses of cyclophosphamide, adriamycin and methotrexate are not as high as in the other phases of treatment.

Oral methotrexate dosing was found to be inconsistent with some clinicians dosing it at 25mg/m<sup>2</sup> and others at 12.5mg/m<sup>2</sup>. In various studies done the main dosage used ranged between 15-25mg/m<sup>2</sup> [8,12,24]. The drug formulation the drug comes in also poses a problem in that it comes as a tablet formulation of 2.5mg in the hospital pharmacy and most private pharmacies requiring most of the patients to take 3-16 tablets once every week.

Anthracyclines have been shown to have cardio toxicity which is related to the cumulative dose of the drug used whereby cumulative doses of less than 400mg/m<sup>2</sup> had a 0.14% risk of causing cardiovascular toxicity and at 550mg/m<sup>2</sup> a risk of 7% [25-27]. However a study done by Nousianen, *et al.* found a decrease in left ventricular ejection fraction after a cumulative dose of 200mg/m<sup>2</sup> however, an increase in atrial natriuretic peptide was evident only in cumulative doses of doxorubicin above 400mg/m<sup>2</sup> [28]. Various studies have also shown age at treatment to be a risk factor with those below four years being at higher risk. The risk has also been found to be greater in females whereby females especially those above twelve years have been found to have twice as high a risk of early clinical cardio toxicity compared to a male of the same age and body surface area [29].

Therefore in our study it can be postulated that 63.1% of the patients stand a low risk of developing cardio toxicity as their cumulative dosages of doxorubicin are between 200-400mg/m<sup>2</sup> while only a small percentage of the patients (10%) stand a significant risk of developing cardio toxicity as their cumulative doses are above 400mg/m<sup>2</sup>.

## Conclusion

The overall adherence to oral chemotherapy in the management of Non Hodgkin's lymphoma in the maintenance phase was found to be 57.9%. This may contribute to the increased risk of relapse in 42.1% of the patients who were non adherent.

The commonest reasons given by patients for failing to take their medication were being unable to afford the medication followed by unavailability of the drug in the hospital or private pharmacies.

Method of acquisition of the oral medications and estimated expenditure on medication per month were found to be significant barriers to adherence. This can be attributed to high costs of oral medication especially 6-mercaptopurine.

Counseling on side effects of the medication was also a significant barrier to adherence suggesting that extensive counseling and parent education on medication use and its side effects were lacking.

The major side effects experienced in order of prevalence were alopecia, change in nail or skin pigmentation, vomiting, mouth ulcers and myelosuppression.

A large number of the patients in this study were found to be taking an inadequate dose of their oral methotrexate due to under dosing or improper administration of the drug. Based on cumulative doses of doxorubicin given, it can be postulated that 63.1% of the patients had a low risk of developing cardiotoxicity while only 10% had a significant risk of developing cardiotoxicity.

## Recommendations

- Similar studies should be carried out in future using large sample sizes so as to detect important associations that may not have been detected in this study
- Further research should be carried out on event free survival and relapse rate in patients with Non Hodgkin's lymphoma and in the maintenance phase of therapy especially in relation to adherence

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