Original Article
Middle East Journal of Cancer 2013; 4(3): 119-124

Lymphoma Prevalence Patterns in Uganda, 1969-2006

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Abstract

Background: Lymphomas are a complex group of malignancies that require advanced technology for proper classification. Unfortunately Uganda, as with numerous other Sub-Saharan African countries, lacks these resources. As a result, lymphoma diagnoses do not follow WHO guidelines.

Methods: Histopathology records at Makerere University College of Health Sciences, Department of Pathology and the population estimates available through the Population Division of the United Nations Department of Economic and Social Affairs (2011) were used to calculate the prevalence of lymphomas in Uganda.

Results: The most common pediatric (age: less than 15 years) lymphoma was Burkitt's lymphoma, followed by lymphoblastic lymphoma. For adolescents and young adults (age: 15 to 24 years), Hodgkin's lymphoma was the leading subtype, followed by lymphoblastic lymphoma. For adults, small lymphocytic lymphoma was the most common subtype, followed by Hodgkin's lymphoma. In this study there was a dip in the prevalence of lymphomas during the period 1979 to 1988, followed by a steady increase. This coincided with the time when Uganda lost many of its experts because of political turmoil and therefore might be due to a lack of clinicians and histopathologists that lead to this decline.

Conclusion: This study highlights the deficiencies in diagnosis of lymphomas, making it difficult to compare with other centers. There is a need to invest in immuno-histochemistry techniques to aid better classification of lymphomas in Uganda.

Keywords: Lymphomas, Malignancies, Uganda

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Introduction

Neoplasms originating in the lymphoid tissue comprise a diverse yet closely related group of neoplasms, including non-Hodgkin's lymphoma (NHL), Hodgkin's lymphoma, multiple coexisting lymphomas, post-transplant lymphoproliferative disorders and acute lymphoproliferative disorders associated with primary immune disorders as well as those associated with HIV and iatrogenic lymphomas.[1] In Uganda, lymphomas

Received: April 30, 2014; Accepted: May 28, 2013

are the most common childhood malignancies with Burkitt's lymphoma accounting for the bulk of cases. Among adults they rank fourth,[2] hence their importance in cancer epidemiology in Uganda. Lymphoma classification is continuously updated as better diagnostic techniques and treatment protocols allow for distinct entities to be defined from broader categories.[3] Although the WHO 2001 and 2008 classifications are a worldwide consensus,[4] the prior diagnoses are difficult to categorize per the new criteria. Additionally developing countries that do not have as many facilities must use the systems that are not in tandem with WHO criteria, making comparison difficult.[5] Unfortunately Uganda, just like most other Sub-Saharan African countries (SSA), has yet to upgrade diagnostic criteria to match that of the WHO.[6] In recent years an increase in incidence and prevalence of lymphomas, particularly in developed countries has been reported.[7-9] Furthermore, HIV/AIDS is reported to increase the incidence and prevalence of certain lymphomas.[10,11] However, reports from SSA are contradictory with some showing an increased incidence whereas others have not shown this change.[2,11,12] The increased availability of highly active anti-retroviral therapy in SSA may see an increment in both incidence and prevalence of lymphomas among persons diagnosed with HIV/AIDS.[2,13] Other changes that have taken place in Uganda such as wars, HIV/AIDS, improved socio-economic status and the rapidly rising population may affect disease epidemiology making a study of the pattern of lymphomas in Uganda over the last three decades worthwhile for future reference.

Materials and Methods

We obtained data on the period prevalence of lymphomas from the archives of the Department of Pathology, College of Health Sciences at Makerere University, which until 2006 was literally the only place with histopathological capabilities within Uganda. As such, specimens were sent from all over the country to this department for diagnosis. We retrieved the histology reports from this department. At the Department of Pathology specimens are cut and stained by hematoxylin and eosin. Sections are examined histolologically under light microscope and diagnosis is made without the help of other ancillary methods.

The data was double entered into SPSS 12 (IBM SPSS) with efforts made to remove duplicate entries.

Age-specific period prevalences were calculated using average population estimates obtained for each pair of years from the Population Division of the United Nations Department of Economic and Social Affairs (2011) as the denominator.[14]

Age at diagnosis was grouped into five-year intervals. The period of diagnosis was categorized into two, yearly intervals from 1969 through 2006 (1969–1970 until 2005–2006). This was done so as to enable us get the approximate period prevalence using the United Nations data.[14] For all periods, the prevalences are expressed per million population.

Results

We included a total of 5439 lymphomas in the study, of which 622(11.40%) were Hodgkin's lymphoma. Unfortunately the diagnosis did not follow the subtypes described in WHO classifications as shown in Table 1.

Age distribution by lymphoma subtype is shown in Table1. The most common pediatric (age less than 15 years) lymphoma was Burkitt's lymphoma, followed by lymphoblastic lymphoma. For adolescents and young adults (age 15 to 24 years), Hodgkin's lymphoma was the leading subtype, followed by lymphoblastic lymphoma. For adults, small lymphocytic lymphoma was the most common subtype, followed by Hodgkin's lymphoma. In the elderly (older than 64 years), small lymphocytic lymphoma comprised the bulk of lymphomas, followed by follicular lymphomas. Unfortunately 4.32% of the cases did not have their ages listed on the pathology reports and they could not be classified by age in this study.

The 5439 patients consisted of 3382(62.18%)

Table 1. Age distribution for the different types of lymphomas.

	Age category (years)																	
Histological diagnosis	**0-4**	**5-9**	**10-14**	**15-19**	**20-24**	**25-29**	**30-34**	**35-39**	**40-44**	**45-49**	**50-54**	**55-59**	**60-64**	**65-69**	**70-74**	**75-79**	**80 +**	**Total**
Burkitt's lymphoma	499	1337	473	77	23	10	11	9	6	3	9	2	3	0	1	1	1	2460
Hodgkin's lymphoma	19	81	96	55	68	55	56	32	37	28	37	6	27	12	8	4	1	622
Non-Hodgkin's lymphoma (NHL)	7	39	30	23	17	19	24	13	10	12	14	7	16	1	6	2	0	240
Follicular lymphoma	14	31	26	15	17	30	25	24	25	26	36	17	30	7	11	1	2	337
Unclassified lymphoma	10	31	21	21	10	22	19	5	23	15	7	10	12	2	6	3	0	217
Lymphocytic lymphoma	24	51	47	38	33	31	26	42	50	44	65	31	48	22	15	7	8	582
Lymphoblastic lymphoma	46	178	117	51	42	36	32	25	24	24	27	20	27	6	10	1	2	650
Centrocytic lymphoma	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	1	3	
Lymphoplasmacytic lymphoma	0	0	0	0	1	1	0	0	1	0	3	0	1	0	0	0	0	9
Immunoblastic lymphoma	0	3	3	1	5	1	3	2	4	2	1	1	0	0	0	1	1	28
Histiocytic lymphoma	0	3	3	3	0	0	5	3	4	2	2	4	3	2	1	0	0	35
Total	619	1754	816	284	216	205	201	155	184	156	202	98	167	52	59	20	16	5204

• NHL were not categorized further showing the challenges of diagnosis and future use of the data in research.

Table 2. Lymphoma period prevalence per million by gender.

sex		**Two-year prevalence**																	
Histological diagnosis		1969-70 %	1971-72	1973-74	1975-76	1977-78	1979-80	1981-82	1983-84	1985-86	1987-88	1989-90	1991-92	1993-94	1995-96	1997-98	1999-2000	2001-02	2003-04	2005-06
Male	Burkitt's lymphoma	11.9	16.3	11.8	9.5	5.7	3.5	5.2	5.4	4.5	3.3	5.0	7.4	9.2	10.1	12.6	7.7	12.7	12.2	12.0
	Hodgkin's lymphoma	6.9	12.4	8.5	3.8	3.1	4.2	1.1	1.1	1.9	0.5	1.3	2.0	3.3	0.8	1.9	1.6	3.4	1.7	1.9
	Non-Hodgkin's lymphoma (NHL)	1.1	3.7	4.1	3.1	0.9	0.5	0.0	0.1	0.3	0.0	0.1	0.3	0.9	0.1	0.0	0.4	1.1	3.0	1.0
	Follicular lymphoma	5.0	6.3	3.9	4.4	5.0	4.4	3.2	2.1	0.1	0.6	0.5	0.2	0.4	1.4	0.8	0.1	0.1	0.2	0.2
	Histiocytic lymphoma	1.5	0.6	1.4	0.9	0.3	0.3	0.2	0.1	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0
	Unclassified lymphoma	5.6	4.3	1.5	2.0	1.9	0.8	1.4	1.7	0.5	1.0	0.8	0.8	0.4	0.4	0.5	0.1	0.0	0.3	0.1
	Lymphocytic lymphoma	4.0	1.8	1.4	2.2	4.5	3.1	5.0	4.9	3.6	3.7	2.9	4.4	2.8	2.9	3.1	0.4	0.4	0.1	0.3
	Lymphoblastic lymphoma	3.2	4.5	5.0	3.6	4.8	4.0	2.7	1.9	1.2	1.2	1.6	2.5	1.9	2.7	3.8	2.9	3.2	3.1	1.1
	Centrocytic lymphoma	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.1	0.1
	Lymphoplasmacytic lymphoma	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0
	Immunoblastic lymphoma	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.7	0.4
Total		39.2	50.1	37.4	29.5	26.0	20.7	18.7	17.4	12.1	10.3	12.3	17.6	18.9	18.6	22.8	13.1	21.0	21.4	17.2
Female	Burkitt's lymphoma	12.0	12.7	5.3	5.4	6.1	2.4	3.5	2.4	4.0	2.0	3.1	5.1	6.7	5.5	8.7	6.2	8.9	7.7	6.6
	Hodgkin's lymphoma	1.5	4.2	4.4	1.8	1.5	1.4	0.3	0.1	0.4	0.5	0.8	0.2	1.4	0.7	1.4	1.3	1.5	1.6	1.0
	Non-Hodgkin's lymphoma (NHL)	0.6	1.0	1.3	1.4	0.9	0.3	0.2	0.0	0.0	0.0	0.0	0.1	0.5	0.0	0.0	0.5	1.0	1.6	0.8
	Follicular lymphoma	3.9	3.8	3.2	2.7	2.4	1.9	1.8	0.7	0.4	0.1	0.2	0.0	0.0	0.6	0.4	0.2	0.0	0.3	0.3
	Histiocytic lymphoma	0.0	0.0	0.4	0.5	0.8	0.3	0.0	0.0	0.0	0.1	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0
	Unclassified lymphoma	2.8	3.2	1.0	2.0	1.4	0.5	0.8	0.4	0.4	0.5	0.4	0.2	0.3	0.5	0.0	0.0	0.0	0.2	0.0
	Lymphocytic lymphoma	2.1	1.6	1.7	2.5	2.2	2.2	2.4	2.0	2.6	1.8	1.5	2.3	1.4	2.1	1.3	0.1	0.3	0.2	0.1
	Lymphoblastic lymphoma	2.0	1.8	3.1	3.2	2.5	1.9	1.8	0.4	0.9	0.5	1.3	0.9	1.8	1.3	1.1	1.8	2.0	1.1	1.2
	Lymphoplasmacytic lymphoma	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.1	0.0
	Immunoblastic lymphoma	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.3	0.6
Total		27.9	28.4	20.4	19.6	16.8	11.0	10.7	6.4	8.7	5.5	7.3	8.9	12.2	10.6	12.8	9.9	13.9	13.1	10.6

•NHL were not categorized further showing the challenges of diagnosis and future use of the data in research.

males and 2023 (37.18%) females. Gender for the remaining cases was not specified. The male/female ratio was 1.67:1.The distribution of lymphoma diagnoses according to gender is shown in Table 2.

The number of new lymphoma patients diagnosed in this department in each two year period ranged from 134 to 469 per year for the 37-year period, with a yearly average of 147 cases. A sharp decline was noted from 1979 to 1990 with the average falling to 85.5 cases. For both genders, Burkitt's lymphoma was the most prevalent lymphoma followed by lymphoblastic lymphoma (Table 2). The overall period prevalence distribution of lymphoma diagnoses made at the department is shown in Figure 1. Figure 2 shows the most prevalent lymphoma diagnosis (Burkitt's lymphoma).

Discussion

Correct diagnosis is a prerequisite for valid estimates of the prevalence and incidence of a disease. Lymphomas can vary from indolent to aggressive types, with various signs and symptoms in different individuals. Prevalence figures cannot be based on clinical history alone. Even when the patient is examined there is a risk of over diagnosis, since there are other conditions that mimic clinical manifestations of lymphomas.[15] A reliable diagnosis is achieved by histopathological examination. On the other hand, if patients with indolent lymphomas are not medically examined by experienced clinicians they will not be referred or have biopsies; hence, they will not be included in a study such as the current one. In Uganda, with its dilapidated healthcare system, history of wars, heavy reliance on traditional healers and poverty,[16] it is likely that patients with disabling symptoms and access to medical care are the ones who seek treatment and undergo biopsies for histological confirmation. Among these, delays in seeking medical care and referrals probably lead to death before the diagnosis is made.[16] Therefore, indolent cases may not present for medical attention while very aggressive ones could have died before diagnosis. In the present study, the diagnosis is with all probability correct as far as the examined lymphoma cases are concerned, but our prevalence figures are likely to be somewhat lower than in cancer surveillance reports that take extra efforts to trace patients in other treatment centers and within communities.

In this study there was a dip in the prevalence of lymphomas during the period 1979 to 1988 followed by a steady increase (Figure 1). This coincided with a time when Uganda lost many of its experts due to political turmoil. Possibly, the lack of clinicians and histopathologists led to the decline in diagnosis and apparent dip in prevalence. Additionally some parts of the country were cut off by armed groups. As such, patients and specimens could not be transported - a factor that could partly account for this decline. A similar trend was observed by Mbuliateye et al. which they attributed to the closure of the Cancer Registry.[17] A marked decline occurred in the 1999-2000 period. However on close inspection a small decline was seen in 1995 as well. The trend

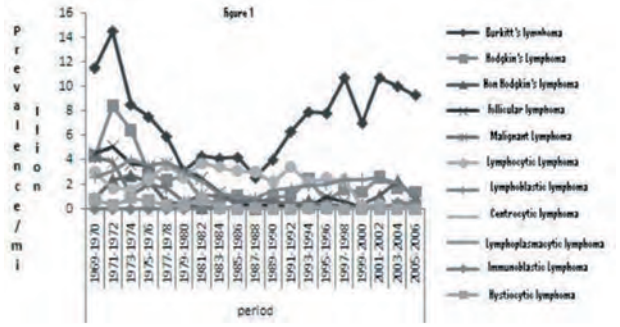

Figure 1. Overall prevalence per million of lymphoma diagnoses at the Department of Pathology, Makerere University College of Health Sciences.

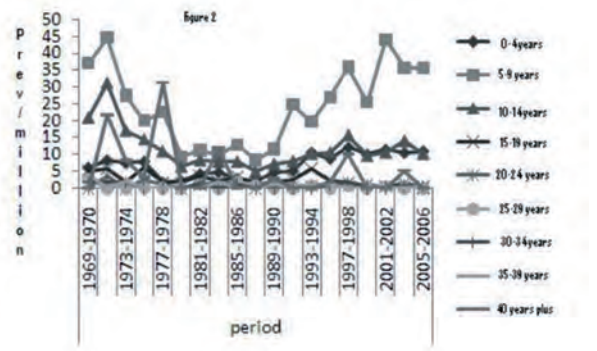

Figure 2. Overall prevalence per million of Burkitt's lymphoma diagnoses at the Department of Pathology, Makerere University College of Health Sciences.

in Figure 1 also showed a decline from 2005-2006. These were election years; the 1999-2000 period was tenser in terms of electoral politics. We could not state that the political atmosphere had anything to do with these changes but it possibly did.

The most common lymphoma was Burkitt's lymphoma, as expected, this was similar to a report from Nigeria,[18] likewise lymphoblastic lymphoma was the next most common lymphoma(Table 1). These results differed with reports from China and USA which showed diffuse large B cell lymphoma as the most common lymphoma.[19,20] Of note, other NHLs have been classified together in addition to another category of unclassified lymphomas. These broad classifications deny us the advantage of knowing the prevalence of non-Burkitt's lymphoma NHL types. This problem has been discussed by Fleming[21] who noted the need to revisit the stored slides for better categorization. Additionally the USA and Chinese studies utilized immunohisto staining, therefore some of the subtypes observed in those studies could have been missed in our study. Given the accepted WHO classification and need to compare the worldwide epidemiology of lymphomas to assist in planning management, we feel there is a need to revisit our stored histological slides and subject them to new diagnostic techniques available in order to align them with the current WHO lymphoma classifications. A case in point is histiocytic lymphomas; in this study we had a couple of cases with this diagnosis. However, it must be noted that true histiocytic lymphomas are rare and require special investigative procedures to enable one reach such a diagnosis with a high degree of certainty.[22] These facilities are lacking in Uganda, hence such a diagnosis is highly questionable.

Hodgkin's lymphoma constituted 11.40% of cases, which was similar to figures from Nigeria, China, South Africa and the USA.[18-20, 23] Therefore it seems Hodgkin's lymphomas occur with nearly equal frequency in these diverse populations. Unfortunately in our study there was no further sub-classification of Hodgkin's lymphoma that matched the WHO classification which is epidemiologically useful.[3] The failure to sub-categorize these cases was due to the lack of immunohistochemistry facilities that would allow for these distinctions, even if only to the hierarchical group 3 level.

All lymphoma diagnoses made were most prevalent among males as can be seen in Table 2. Reports have shown that certain lymphomas such as nodular lymphocyte predominant Hodgkin's lymphoma are more common among females than males of the black race.[20] Unfortunately in our study, diagnoses such as NHL, malignant lymphomas and Hodgkin's lymphoma were not informative and therefore we were unable to classify them. Thus we could not make a comparison between genders for the different sub classifications.

There is a need to use modern techniques to re-categorize lymphomas according to the WHO classification in order to allow us to compare our findings with other centers.

Acknowledgement

We are sincerely grateful to our colleagues at the Department of Pathology, Makerere University College of Health Sciences.

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