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Non Hodgkin Lymphoma and Related Factors in Patients with Peripheral Lymphadenopathy in Lubumbashi (DR Congo)

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Authors' contributions

This work was carried out in collaboration between all authors. Authors CK and CM conceived and designed the study. Authors CK, Marc Kashal, EK and VK conducted and collected data. Authors CK, OM, MM, Michel Kabamba, EM, HNS, OL, FM and CM contributed to data analysis, interpretation and manuscript review. Authors CK, MM and TB wrote the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Lymphadenopathy refers to the condition in which lymph nodes become abnormal with regards to the size, consistency, tenderness, and may be one of the the symptoms of many diseases. Unfortunately striking differences still exist with respect to reliability of NHL diagnosis between developed and developing countries. However some authors think epidemiological factors would exist to orientate diagnosis of NHL. Thus this study aimed to determine sociodemographic, clinic and biological factors associated with NHL in patients with peripheral lymphadenopathy in the department of internal medicine at the University of Lubumbashi Clinics.

Materials and Methods: This is a cross-sectional study on superficial lymphadenopathy observed over a period of 30 months from November 2013 to April 2016 at the University of Lubumbashi Clinics. Parameters studied included gender, age, localization and clinical characteristics of superficial lymphadenopathy; biological parameters and pathologic diagnosis were determined by lymph nodes biopsy.

Results: Data of 52 patients was collected and 40.40% of these patients had NHL as pathologic diagnosis. Some of variables studied presented a significant statistical association and included age ≥ 50 years old (p = 0.0072), male gender (p= 0.0381), inguinal location (p =0.0081), multifocal location (p = 0.0101), painless (p= 0.0360), HIV serology (p= 0.0192) and leukocytosis (p=0.0022). After logistic regression, NHL explicative variables: male gender, painless and leukocytosis were significant.

Conclusion: These related factors can be used as elements to orientate the diagnosis for our health facilities and would contribute to early NHL diagnosis for patients with lymphadenopathy in low-income countries like the DR Congo.

Keywords: NHL; related factors; superficial lymphadenopathy; epidemiology; Lubumbashi.

ABBREVIATIONS

NHL : Non Hodgkin Lymphoma
HIV : Human Immunodeficiency Virus
AIDS : Acquired Immune Deficiency Syndrome
DR Congo : Democratic Republic of Congo
HL : Hodgkin Lymphoma
IL : Infectious Lymphadenitis
RH : Reactive Hyperplasia
UM : Undifferentiated Malignancy
ST : Secondary Tumor

1. INTRODUCTION

Lymphadenopathy refers to the condition in which lymph nodes become abnormal with regards to the size, consistency, tenderness, and it may be one of the symptoms of many diseases. The history of the patient should be considered carefully because it may provide clues of underlying disease. It usually points infection in younger adults although a malignancy is important differential in old age [1].

Malignant lymphoma is a primary malignant neoplasm of lymphoid tissue arising from the expansion of malignant transformed lymphocytes which may contain one or more genetic abnormalities [2]. Non Hodgkin Lymphoma (NHL) is a heterogenous disease resulting from the malignant transformation of lymphocytes and includes multiple subtypes each with specific molecular and clinical characteristics [3].

Although accurate estimates are difficult, given the paucity of information, it is likely that approximately 30,000 cases of NHL occur in the equatorial belt of Africa each year and these tumors are among the top ten causes of cancer in this geographical region. The fraction associated with AIDS is not available, but may be as high as 50%, although it appears to vary markedly throughout the region and is different among children and adults [4-6].

Meaningful research on NHL in Africa cannot be conducted without accurate diagnosis. Unfortunately, striking differences still exist with respect to the reliability of NHL diagnosis between developed and developing countries, due partly to limited number of hematopathologists and partly to the lack of special reagents, such as monoclonal antibodies and molecular probes that are indispensable to an accurate diagnosis based on the World Health Organization classification of hematopoietic and lymphoid tissues [7]. Also, the resource limitation (human and material) in Africa restricts the ability to make an accurate diagnosis early in the

course of the disease [8]. However some authors think that epidemiological factors would exist to orientate NHL diagnosis [9-10].

Thus this study aimed to determine sociodemographic, clinical and biological factors associated with NHL in patients with peripheral lymphadenopathy in the department of internal medicine at the University of Lubumbashi Clinics.

2. MATERIALS AND METHODS

2.1 Type and Study Period

This is a descriptive and transversal study on patient with superficial lymphadenopathy who had consulted in the department of internal medicine at the University of Lubumbashi Clinics (DR Congo) from 1st November 2013 to 30 April 2016.

2.2 Study Population

We have proceeded by a convenience sampling including all patients with superficial lymphadenopathy seen at the internal medicine outpatient department or those admitted in the department of internal medicine at the University of Lubumbashi Clinics where 52 patients had presented with lymphadenopathy. We included, any patient with hypertrophy affecting one or more palpable superficial lymph nodes in the cervical, axillary or inguinal area, measuring more than one centimeter in diameter, irrespective of the gender. We have retained the age above 15 for our series. We excluded, all patients on TB treatment and/or on antimitotic treatment. The study was done using and analyzing patients medical records including sociodemographic parameters (age, gender), clinical description of lymphadenopathy (localization, consistency, mobility, sensibility), biological (hemoglobin, red cells, white cells, platelets, HIV serology) and pathologic parameters.

2.3 Biologic and Histopathology Analysis

1) HIV infection diagnosis: HIV serology was determined by a screening rapid test: Determine TM HIV-1/2 (Alere) and positive cases were confirmed by ELISA: Vironostika and Enzygnost done on IMMUNOWASH type WELLWASH 4 MK 2 N°SERIE 006-9-7943.
2) Bacteriologic analysis of infectious lymphadenopathy: Secretions culture was done on an ordinary microbial culture medium: Sabouraud and Loweisten.
3) Full Blood Count: Blood analysis was done using hematology automate ABX MICROS 60 № SERIE 8050S85648 (Table 1).
4) Histopathologic diagnosis was obtained from the histopathologic department of the University of Lubumbashi Clinics. All slides were made from paraffine embedded blocks, and then stained with hematoxylin and eosin. Immunohistochemistry, cytogenetics and molecular diagnostic techniques like lymphocyte receptor gene rearrangements were not employed as these are not available in our laboratory. The diagnosis of Hodgkin's lymphoma was based on a morphological diagnosis (research for cells heterogeneity and the tumor cell: Reed-Steinberg cells).

Table 1. Values of full blood count were categorized as follow [11]

Gender	RCC (10^{12}/L)	HB (g/dl)	WCC (10^{9}/L)	Platelet (10^{9}/L)
Male	3.3-6.4	10-18.4	1.9-10.1	120-443
Female	3.1-6.0	10.3-17.1	2.2-7.8	150-436

1) Hemoglobin (Hb):
• <10 g/L: values considered as anaemia for male gender
• <10.3 g/L: values considered as anaemia for female gender
2) White cells count (WCC):
• >10.1 × 10^{3}/mm^{3}: values considered as leukocytosis for male gender
• >7.8 × 10^{3}/mm^{3}: values considered as leukocytosis for female gender
3) Red cells count (RCC):
• <3.3 × 10^{6}/mm^{3}: values considered as erythropenia for male gender
• <3.1 × 10^{6}/mm^{3}: values considered as erythropenia for female gender
4) Platelets count:
• <120 × 10^{3}/mm^{3}: value considered as thrombocytopenia for male gender
• <150 × 10^{3}/mm^{3}: value considered as thrombocytopenia for female gender

2.4 Data Statistics Analysis Technique

Different data collected were coded then captured on a computer and statistical analysis was performed on Microsoft Excel 2010 for encoding of data and Epi Info7® for determining frequencies. Statistical comparisons between diagnoses and socio-demographic, clinical and biological parameters have been made and the Fischer exact test or Chi square test was used for comparison of frequencies with a significant level of $p < 0.05$.

A logistic regression with a step by step method by WALD using IBM SPSS Statistics version 19 software, has allowed to establish relations between sociodemographic variables, clinical characteristics of superficial lymphadenopathy and associated signs and biologic parameters (selected variables based on p criterium <0.05) and the dependent variable (NHL) of the study such as risk factors of NHL occurrence.

2.5 Ethics Considerations

The study was approved by the Ethical Committee s of Lubumbashi' University. For ethics and code of practice reasons and trying to avoid stigma, data were collected in such a manner that patients remained anonymous after obtaining their consent wich has been collected and preserved by the authors.

3. RESULTS

During this study, 52 patients were listed and Table 2 shows sociodemographic, clinical characteristics and biological parameters of these patients with peripheral lymphadenopathy. Among these patients, 21 (40.40%) of them were diagnosed with NHL with a sex ratio M/F estimated at 2.5 and a median age of 48 years.

We notice there is a significant statistical association between NHL diagnosis and these variables: Age ≥50 years (p=0.0072), male gender (p=0.0381), inguinal location (p=0.00681), multifocal location (p=0.0101), painless (p=0.0360), HIV serology (p=0.0192), leukocytosis (p=<0.0001).

Table 3 shows, after logistic regression, NHL significant variables such as the male gender, painless and leucocytosis were significantly associated to the occurrence of NHL with the adjusted Odds Ratios respectively: 10.128 (IC: 1.644-62.389 to 95%), 10.128 (IC: 1.644-62.389) to 95%) and 50.049 (IC: 5.312-471.524 to 95%).

Table 2. Superficial lymphadenopathy patients with NHL as pathologic diagnosis

Variable	NHL (n=21)		Others* (n=31)		Total (n=52)		OR [ICà95%]	p
	n	%	n	%	N	%		
Sociodemographic characteristics								
Age ≥50 years	10	47.6	4	12.9	14	26.9	5.9 [1.3-31.5]	0.0072
Male gender	15	71.4	13	41.9	28	53.8	3.5 [1.1-11.3]	0.0381
Topography								
Cervical	21	100.0	26	83.9	47	90.4	Undefined	0.0653
Inguinal	13	61.9	7	22.6	20	38.5	5.6 [1.6-18.8]	0.0081
Axillary	10	47.6	7	22.6	17	32.7	3.1 [0.9-10.4]	0.1124
Multifocal location	13	61.9	7	22.6	20	38.5	5.5 [1.6-18.8]	0.0101
Clinical characteristics								
Painless	15	71.4	13	41.9	28	53.8	3.5 [1.1-11.3]	0.0360
Mobility	20	95.2	25	80.6	45	86.5	4.6 [0.5-231.6]	0.1352
Hard	14	66.7	21	67.7	35	67.3	0.9 [0.3-3.1]	0.8257
Biological parameters								
HIV+ serology	3	14.3	14	45.2	17	32.7	0.20 [0.0-0.9]	0.0192
Anemia	13	61.9	12	38.7	25	48.1	2.6 [0.8-8.0]	0.1000
Leukocytosis	13	61.9	3	9.7	16	30.8	15.2 [3.4-66.7]	<0.0001
Thrombocytopenia	6	28.6	13	41.9	19	36.5	0.1 [0.2-1.8]	0.3260
Erythropenia	10	47.6	9	29.0	19	36.5	2.2 [0.7-7.1]	0.1720

**Others: HL, IL, RH, UM, ST*

Table 3. Logistic regression of NHL significant variables

Non hodgkin lymphoma significant factors	A	S.E.	Wald	p	Exp(B)	C.I. for Exp(B) 95%	
						inferior	superior
Male gender (x1)	2.315	0.928	6.230	0.013	10.128	1.644	62.389
Painless (x2)	2.315	0.928	6.230	0.012	10.128	1.644	62.383
Leukocytosis (x3)	3.913	1.144	11.691	0.001	50.049	5.312	471.524
Constant	-10.699	3.101	11.699	0.001	0.000		

A: regression coefficient; S.E.: regression coefficient standard error ; Wald :Wald test ; p : p-adjusted value; Exp(B) : adjusted Odds Ratio, C.I. :Exp(B) confidence interval

4. DISCUSSION

During some clinical circumstances, lymph nodes present morphologic and pathologic variations. Some of these clinical situations include malignant proliferation, within these lymph nodes or extension through lymphatic and/or blood stream, of lymphoma developed within the lymph node or distant organ as seen in case of NHL [12].

In our series, 52 patients with superficial lymphadenopathy were listed and 21 (40.40%) had NHL as a pathologic diagnosis. Several authors confirm that this incidence of NHL has been increasing since 1970s across all region and races [9,13-19] and Africa isn't exempted if we refer to Unwin et al. study in Ethiopia [20] and results obtained in our study.

Some studies done on NHL, report, in general a sex ratio in favor of male gender varying between 1.16 to 2 [21-23] but these results seem slightly low compared to our observation.

Even though the median age in our study is slightly higher compared to Isikodogodan et al. in Tunisia [21], this one seems to confirm Lukic et al. theory that estimate the age> 40 would be a predictive factor for malignancy for superficial lymphadenopathy patients [24]. And other authors have established the level of malignancy could become more and more frequent as superficial lymphadenopathy patient are getting older [25-26].

It is nevertheless important to say that some authors like Swerdlow et al. and Naresh et al. think it will be difficult to conduct quality studies on NHL in Africa given the difficulty to make the diagnosis in this part of the world [7-8]. However, some factors have been considered important in NHL epidemiology [9-10,27] and that despite difficulties due to human and material resources. In this study, some factors presented significant statistic correlation with NHL (age ≥ 50 years, male gender, inguinal location, multifocal location, painless, HIV serology and leukocytosis) as pathologic diagnosis. The logistic regression of these significant statistic variables have highlighted that the male gender, the painless and leukocytosis in our patients might be explicative factors for NHL occurrence with a respective ORa of 10.128, 10.128 and 49.451.

The associated factors obtained in our study are also found by other authors. Huh et al. believe that age and sex are important factors in the epidemiological of NHL and report that NHL's incidence increases as the age is advancing [28]. For Yoon et al. and Kim et al., NHL incidence continues to increase with age in men [29-30] and is more common in man than women according to Park et al. [27]. Concerning clinical characteristic, it has been recognized that the painless is regularly encountered in NHL as stipulated by Bazemore et al. and Fijten et al. in their studies [31-32]. As for the biological parameters, extreme increase in the total number of leukocytes can be found in myeloproliferative disorder [33].

5. CONCLUSION

52 patients with superficial lymphadenopathy were recorded in our series and several NHL associated factors were observed (age ≥ 50, male gender, inguinal location, multifocal location, painless, HIV serology and leukocytosis).With these associated factors, we believe that it would be possible to have socio-demographic, clinical and biological features that can guide healthcare providers in unsupported technical facilities and will assist in diagnosis of NHL especially in areas where diagnostic facilities are not readily available and can contribute to an early diagnosis of NHL of patients with superficial lymphadenopathy in low-income countries like the DR Congo.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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