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Original Article

Epidemiological, Clinical and Therapeutic Aspects of Chronic Lymphoid Hemopathies Observed at the National Reference University Hospital Center of N'Djamena

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Abstract *- Chronic lymphoid hemopathies (CHL) remain a major public health problem in low-income countries. It is therefore important to determine the epidemiological and clinical characteristics and to contribute to the care.*

This study aims to determine the epidemiological and clinical profile and to contribute to better management of HLC in Chad.

The aim was to determine the epidemiological, clinical, therapeutic profile of chronic lymphoid hemopathies (CLH) and the viral factors linked to the genesis of HLCs at the CHU-RN of Ndjamena in Chad.

A descriptive cross-sectional study over two and a half years, from October 2017 to March 2020, at the Hematology Unit of the National Reference University Hospital Center (CHU-RN) of Ndjamena. Were included patients in whom the diagnosis of chronic lymphoid hemopathy had been made.
Ninety-eight (98) cases of haematological malignancies were recorded out of 531 haematological consultations, including 66 (12.43%) CLH and 67.35% of haematological malignancies with an annual incidence of 26.4 cases. Chronic lymphocytic leukemia (CLL) was 56.06% (n=37) followed by 25.76% (n=17) Malignant non-Hodgkin's lymphoma, 15.15% (n=10) Hodgkin's lymphoma and 3.03 % (n=2) cutaneous lymphoma. A male predominance was observed for all types of CLH. The most represented age groups were those of 51 to 60 years for CLL and 11 to 20 years for lymphomas.

This study made it possible to have a piece of better epidemiological knowledge and the viral factors related to the genesis of CLH at the CHU-RN of Ndjamena. It revealed difficulties in biological diagnosis and management, in particular the initiation of chemotherapy.

Keywords - *Chronic lymphoid hemopathies, Viral factors, CHU-RN, Ndjamena, Chad.*

I. INTRODUCTION

Chronic lymphoid hemopathies are cancerous pathologies developed at the expense of the lymphoid tissue. They include many entities, each with specific clinical, cytological, histological and therapeutic characteristics [1-3]. Although less common than tropical diseases (infectious and parasitic diseases), they occupy an important place in our hospital practices.

They are the most common haematological malignancies in Western countries and in most African countries [4-8]. They represent approximately 3.4% of cancer cases worldwide [9].

The etiologies of these conditions are not known, but many chronic viral or bacterial infections are incriminated as well as several factors with complex interactions [10, 18, 19, 20].

In Chad, although many cases of chronic lymphoid hemopathies are encountered in our hospitals and which pose enormous diagnostic and therapeutic difficulties, studies on these pathologies are almost non-existent. It is in this context that the present study, the first of its kind, aims to determine the epidemiological and clinical aspects of chronic lymphoid hemopathies and the serological status of patients observed at the National Reference University Hospital Center (CHU-RN) of N'Djamena.

II. MATERIAL AND METHODS

A. Type and period of study

This was a descriptive cross-sectional study over two and a half years, from October 2017 to March 2020, conducted at the Hematology Unit of the CHU-RN of Ndjamena.

B. Study Population

The study involved all patients followed in haematology consultation during this period and meeting the following inclusion criteria:

Chronic lymphocytic leukaemia (CLL): the diagnosis of CLL was retained on the basis of age ≥ 50 years, blood hyperlymphocytosis greater than 5000/mm3 at least twice consecutively on the blood count, associated with hyperplasia lymphocyte consisting of small lymphocytes with a mature appearance accompanied by the presence of Gümprecht shadows on the blood smear, and incidentally immunophenotyping when the means allow it.

Lymphomas: diagnosed mainly by a histological study of lymph node biopsy, surgical excision of pieces of an organ tissue or skin lesion.

C. Laboratory Tests

The biological product we examined was whole blood, serum or plasma.

Screening for chronic lymphocytic leukaemia (CLL), malignant non-Hodgkin's lymphoma, Hodgkin's lymphoma and finally cutaneous lymphoma was carried out with the usual laboratory diagnostic means: complete blood count (Blood Formula Numeration (BFN), blood smear) and cytology.

a) BFN assessment (blood count)

An NFS assessment is the quantitative (count) and qualitative (formula and assessment of cell morphology) analysis of the figurative elements of the blood: red blood cells, white blood cells and platelets. This BFN is performed automatically using the Dx 120 Pentra (HORIBA) and the XLR 80 Pentra (HORIBA). These two devices also make it possible to measure blood counts constants as well as the determination of the rate of reticulocytes.

D. Thin smear technique

- The drop of blood must be half the size of that used for the thick drop.
- Apply the edge of another glass slide to the drop of blood at a 45° angle, let the blood spread by capillary action along the edge of the blade.
- Push the blade forward while keeping it at the same angle.
- It is essential to push the blade all at once and without stopping or starting again; the blood should follow the blade and not be pushed by it.
- A well-done smear should consist of a thin, even layer of blood, with the tip of the smear not touching the edge of the slide. Dry the smear immediately by shaking the slide or placing it in front of a fan.

E. May Grunewald Giemsa stain (MGG)

- For better staining of the smears, the pH of the solution should be adjusted to 7.2.
- Staining can be fast or slow depending on whether ready-to-use May-Grunwald solutions or Giemsa stock solution are used or diluted 1/10 (1 volume of Giemsa to 9 volumes of distilled water).

MGG staining steps:

- Cover the smear with the May-Grünewald solution, leave it to act for 2 to 3 min.
- Discard the dye by washing with water.
- Cover the smear with Giemsa solution and leave to act for 5 min.
- Discard the stain by washing with water, drain and dry the stained slide between two sheets of blotting paper or at laboratory temperature.

The microscopic observation of the MGG colouration is done with the x100 objective with immersion oil.

Screening for infectious markers was carried out according to the recommendations of the National Blood Transfusion Program and the National Program for the Fight against AIDS and STIs, which recommends the use of the following rapid tests:

Test for the diagnosis of HIV infection, the presence of HIV1 and HIV2 Antibodies was sought with a rapid test Determine ½ (Alere Medical Co.Ltd.).

Hepatitis B surface Antigen (HBsAg) infection screening test was tested using the HBsAg One Step SD Bioline rapid test (Whole blood/Serum/Plasma). Test for screening for HCV infection Anti-HCV Antibodies was sought with the HCV One Step SD Bioline (Whole blood/Serum/Plasma).

F. Data analysis

The data were encoded and analyzed using Excel and Word 2016 software. From a statistical point of view, we used the average standard deviation to look for an association between sociodemographic parameters and lymphoid hemopathies wanted chronicles.

G. Ethical Considerations

The study was approved by the ethics committee of the University of N'Djamena. Research authorization was obtained from the Dean of the Faculty of Human Health Sciences and the Director of the National Reference General Hospital for this work.

Thus, for ethical reasons, the processing of data was done anonymously for all patients after obtaining their consent.

III. RESULTS

Out of 531 haematological consultations listed during the study period, 98 cases of malignant hemopathies were collected, including 66 cases of chronic lymphoid hemopathies representing 12.43% of haematological consultations and 67.35% of all malignant hemopathies with an annual incidence of 26.4 cases. Among these cases, chronic lymphocytic leukaemia (CLL) was mainly represented with 37 cases (56.06%) against 29 cases (43.94%) of lymphomas, including 17 cases (25.76%) of non-Hodgkin lymphomas (NHL), 10 cases (15.15%) of Hodgkin's lymphoma (HL) and 2 cases (3.03%) of cutaneous lymphoma (CL). Globally considered chronic lymphoid hemopathies involved all age groups in our study. The most represented age groups were those from 51 to 60 years old for CLL with an average age of 59.59 ± 8.85 years and from 11 to 20 years old with an average age of 32.34 ± 16.13 years for lymphomas. No case of CLL has been observed before the age of 30. The average age for all chronic lymphoid hemopathies combined was 47.62 ± 18.47 years, with extremes ranging from 12 to 75 years. We note a predominantly male distribution for all chronic lymphoid hemopathies. Patients residing in Ndjamena were mainly represented with 59.09%. The rest were spread over all the regions of Chad. The dominant professions were made up of farmers and herders. The serological status (Infection Transmissible by Blood Transfusion) of patients systematically evaluated had reported two cases of HIV and two cases of hepatitis B. The average time between the onset of symptoms and the consultation was 17 months. The main physical signs were lymphadenopathy, splenomegaly and mucocutaneous pallor. Fifty-one (51) patients out of 66, representing 77.27%, could not have access to the specific treatment. Only 15 (23.73%) patients had access to treatment, including 8 cases of CLL and 7 cases of lymphoma. All lymphoma cases were treated with cyclophosphamide, vincristine and prednisone (COP). For CLL cases, 3 patients were treated with Fludarabine-Cyclophosphamide, 3 others with chloraminophen and 2 with the COP protocol.

A. Distribution of the Prevalence of Hemopathies

Fig. 1 illustrates the repair of the prevalence of chronic lymphoid hemopathies. Chronic lymphocytic leukaemia was predominant, followed by non-Hodgkin's lymphoma.

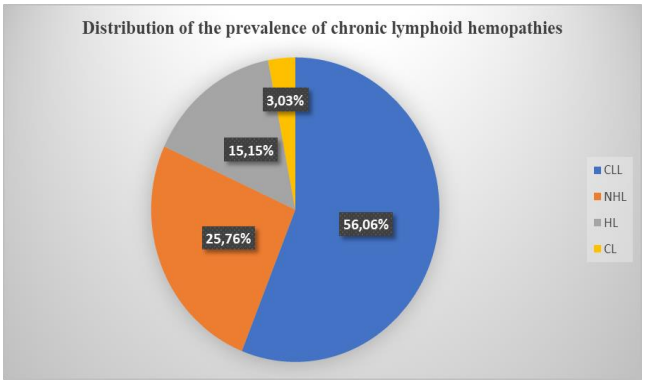


Fig. 1 Prevalence of chronic lymphoid hemopathies

CLL: Chronic Lymphoid Leukemia
NHL: Non-Hodgkin lymphoma
HL: Hodgkin's lymphoma
CL: Cutaneous Lymphoma

B. Distribution of Patients by Age Group and Type of Blood Disease

Fig. 2 illustrates the distribution of patients by age group and type of blood disease. CLL was highest in the age group of 51-60 years (12), followed by 61-70 years (9).

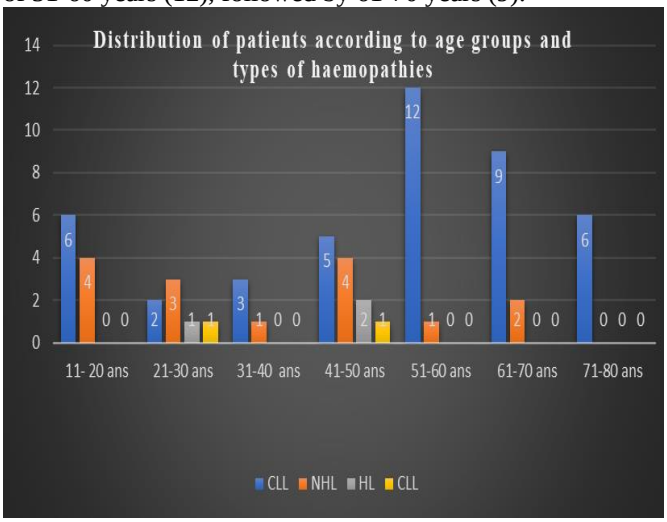


Fig. 2 Distribution of patients by age group and type of blood disease

C. Distribution of Patients According to Gender and Types of Hemopathies

Fig. 3 illustrates the distribution of patients by gender and type of blood disease. The male sex was the most affected by CLL.

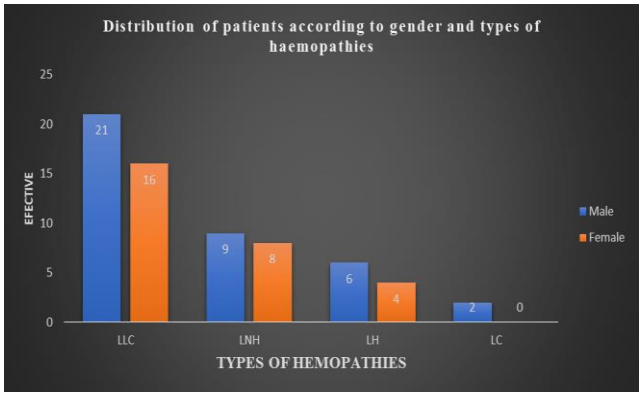


Fig. 3 Distribution of patients according to sex and type of hemopathies

D. Distribution of Patients According to their Profession

Table 1 shows the distribution of patients by profession. The dominant professions were made up of farmers (21.21%) and breeders (18.18%).

Table 1. Distribution of patients by profession

Profession	Frequency	Percentage (%)
Farmer	14	**21.21**
Breeder	12	**18.18**
Trader	9	13.64
Functionary	8	12.12
Worker	8	12.12
Household	7	10.61
Neither	8	12.12
Total	**66**	**100**

E. Distribution of Patients According to Clinical Manifestations

Fig. 4 illustrates the distribution of patients according to clinical manifestations. The most dominant clinical manifestations are lymphadenopathy, followed by conjunctival pallor.

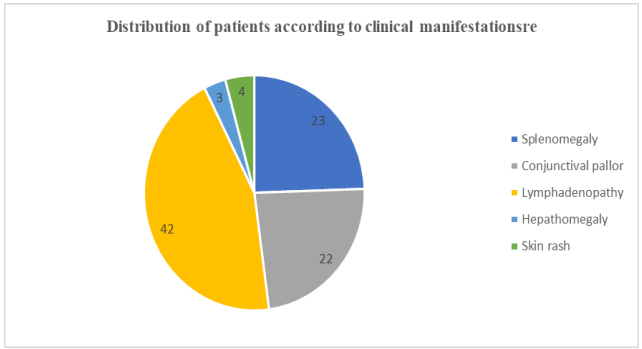


Fig. 4 Distribution of patients according to clinical manifestations

F. Distribution of Patients Based on Blood Formula Numeration Data

Table 2 shows the distribution of patients according to Blood Formula Numeration (BFN) data. Hyperleukocytosis was between 25,000-50,000 GB/mm^3 (29.73%) and the platelet count was greater than 150,000/mm^3 (37.84%).

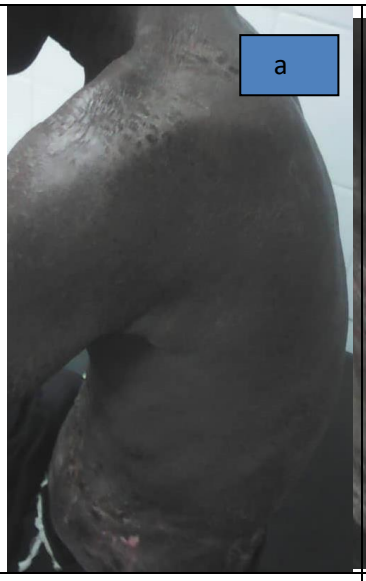
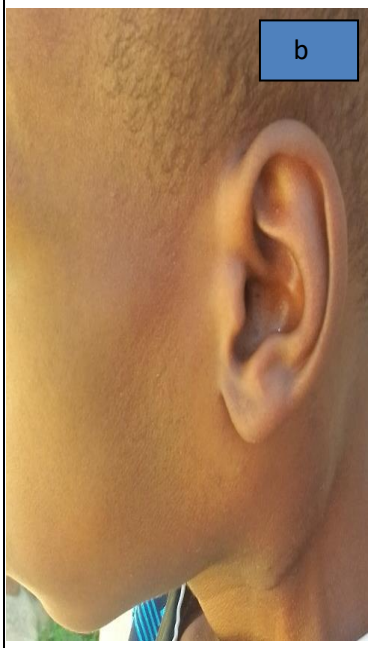
Table 2. Distribution of patients based on Blood Formula Numeration data

Blood Formula Numeration (BFN)	Limite	Effective	Percentage (%)
White Blood Cells (/mm^3)	10 000-50 000	9	24.33
	51 000-100 000	16	43.24
	101 000-200 000	8	21.62
	>200 000	4	10,81
	Total	**37**	**100**
Hemoglobin (g/dL)	<5,99	5	13.51
	6-9,9	15	40.54
	10-11,9	11	29.73
	>12	6	16.22
	Total	**37**	**100**
Platelet (/mm^3)	<100 000	12	32.43
	100 000-150 000	11	29.73
	>150 000	14	37.84
	Total	**37**	**100**
Lymphocyte	5 000-15 000	7	18.92
	15 000-25 000	9	24.33
	25 000-50 000	11	29.73
	50 000-100 000	6	16.21
	>100 000	4	10.81
	Total	**37**	**100**
Neutrophil	<20	7	18.92
	20-40	13	35.13
	>40	17	45.95
	Total	**37**	**100**
Eosinophil	<2	8	21.62
	2-5	14	37.84
	>5	15	40.54
	Total	**37**	**100**
Basophil	<1	6	16.22
	1-5	19	51.35
	>5	12	32.43
	Total	**37**	**100**

G. Macroscopic Characteristics of Cutaneous Lymphomas and Hodgkin's Lymphomas

The photos (a, b) in Table 3 show the macroscopic characteristics of the cutaneous lymphomas and Hodgkin's lymphomas of the patients seen in medical consultation during the study.

Table 3. Macroscopic characteristics of cutaneous lymphomas and Hodgkin's lymphomas

1	a: Cutaneous lymphomas		
2	b: Hodgkin's lymphomas		

IV. DISCUSSION

The limits of our study are at several levels since this work is the first of its kind in Chad and moreover took place in a single health structure at the national level.

The under-equipment of our laboratories makes immunohistochemistry, immunophenotyping and cytogenetic examination impossible on site. Similarly, the financial difficulties of most patients make these expensive examinations carried out in collaboration with laboratories outside the country unfeasible.

The high cost and the unavailability of anti-cancer drugs on site have contributed to underestimating the number of patients treated.

These reasons, associated with the absence of information intended for the general public on the existing structure, but also the fact that a large number of patients diagnosed outside Chad are not included in our series, have contributed to underestimating the frequency of these pathologies in the Chadian population.

Nevertheless, this study, the first of its kind in Chad, has made it possible to put the spotlight on these somewhat unknown pathologies and to rank them in the narrow list of cancers in our country.

The annual incidence was 26.4 cases. Our result is similar to those obtained by Moueleu et al. in Cameroon, who reported an incidence of 26.3 cases per year [7]. However, lower than that of N'Dhatz et al. in Ivory Coast, who reported an incidence of 35.9 cases per year [11]. But much higher than that of Ngolet et al., in Congo Brazzaville and Koulidiaty et al., in Burkina-Faso who had respectively noted an incidence of 15 cases per year and 14.4 cases per year [6,8]. This result allows us to affirm that chronic lymphoid hemopathies occupy a significant place compared to infectious pathologies, which are legion in our hospital structures.

Chronic lymphoid leukaemia (CLL) represents the most frequent form of chronic lymphoid hemopathy with 37 cases or 56.06%, followed by non-Hodgkin's lymphoma (NHL) with 17 cases (25.76%), Hodgkin's lymphoma (LH) with 10 cases (15.15%) and cutaneous lymphoma (CL) with 2 cases or 3.03%. These results are comparable to those of Moukaila et al., in Niger [12], who recorded a predominance of CLL with 65.22%, followed by NHL with 23.91%. However, Moueleu et al., in Cameroon [6], noted a predominance of NHL with 53.6%, followed by LLC with 21.6%. This diversification of the distribution of cases in Africa goes contrary to European publications, which reveal a predominance of non-Hodgkin lymphomas [3,4,13,21,22]. This could be explained by the fact that European authors have more appropriate means of exploration, allowing better identification, regular monitoring and appropriate classification of the different types of lymphoma.

Chronic lymphoid hemopathies affect all age groups in our series, such as those reported on the continent and in the West [3-7,10,14, 23-25]. The average age of diagnosed cases was 47.62 ± 18.47 years, with extremes ranging from 12 to 75 years. The most affected age group was between 51 and 60 years old. Our results are comparable to those of Moueleu et al., in Cameroon, who noted an average age of 47.5 years [7] but lower than that of Smith et al., in the United Kingdom, who reported an average age of 70.1 years [4]. This difference in age could be explained by the fact that in Africa, the population is predominantly young.

The predominantly male distribution in our study is consistent with the literature [15]. However, Ngolet et al., in Brazzaville, had reported a predominantly female distribution [6].

The majority of our patients resided in the capital Ndjamena. N'Dhatz et al., in Ivory Coast, had made the same observation [11]. However, this observation is not specific to chronic lymphoid hemopathies. The higher level of information/education and greater accessibility to healthcare facilities in our capitals could explain this situation.

We noted a predominance of agro-pastoral professions. The same observation was made by Moueleu et al. in Cameroon [7], who had noted a predominance of agro-pastoral professions. However, Malam-Abdou et al., in Niger [16], reported a predominance of housekeeping. These disparities observed in African studies make it difficult to precisely identify possible determinants of the disease.

The serological status systematically evaluated in our study series had revealed two cases of HIV and five cases of hepatitis B. The association of these infections in chronic lymphoid hemopathies in our country is little evaluated. However, it is well known. Specified in the literature that viral factors figure prominently in the genesis of malignant pathologies, in particular blood diseases.

The average time between the onset of symptoms and the consultation was 17 months. Malam-Abdou et al., in Niger [16], had noted an average delay of 24 months, much higher than our study. This could be explained by the first-line recourse to traditional healers but also to socio-cultural constraints that suggest mystical causes, but also to the geographical and financial inaccessibility of specialized health structures and the ignorance of patients.

Tumour syndrome and the anaemic syndrome were the main forms of clinical presentation of our cases. These clinical signs have also been reported in African studies conducted by Koulidiati et al., in Burkina-Faso and Ngouadjeu et al., in Cameroon [6,59].

In our study series, 51 patients out of 66, representing 77.27%, could not have access to specific treatment due to the non-availability of drugs but, above all, because of the high cost of anti-cancer drugs, inaccessible for the vast majority. Of our patients. The non-subsidization of cancer treatments by the State and the non-existence of a social security system are all factors that have had an impact on the early start of treatment and which may have darkened the prognosis. This observation challenges the State to become more involved in the management of the treatment of haematological malignancies because patients pay a heavy price.

V. CONCLUSION

Le résultat de cette étude montre que hémopathies lymphoïdes chroniques ne sont pas aussi rares qu'on pourrait le penser au Tchad. Cette étude a également permis d'avoir une meilleure connaissance épidémiologique et les facteurs viraux liés à la genèse des hémopathies lymphoïdes chroniques au CHU-RN de Ndjamena. Elle a révélé des difficultés dans le diagnostic biologique et la prise en charge notamment la mise en route de la chimiothérapie. Un nombre sans doute plus élevé de cas a pu échapper à notre étude pour des raisons techniques et de gestion hospitalière d'informations médicales. Le retard de consultation et de diagnostic était à l'origine des formes avancées de la maladie. Beaucoup reste encore à faire quant au plateau technique et à la prise en charge thérapeutique très coûteuse face aux maigres ressources de nos populations, ce qui du coup réduit considérablement la survie des patients.

VI. ACKNOWLEDGMENTS

We would like to thank the Dean of the Faculty of Human Health Sciences (FSSH) of the University of N'Djamena, the Director of the National Reference University Hospital Center (CHU-RN) and the ethics committee for having authorized this research. Our thanks also go to the patients who agreed to participate in this study.

VII. AUTHORS' CONTRIBUTIONS

Mbanga Djimadoum, Bessimbaye Nadlaou designed the study, processed the data, wrote the manuscript and researched the literature; Lopiagoto Kemteud Blaise collected the data. All authors contributed to the conduct of this work. All authors also declare that they have read and approved the final version of the manuscript.

VIII. CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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