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Clinical, biological, therapeutic and evolving profile of malignant hemopathies in adults at the central hospital of Yaounde

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Abstract

Malignant hemopathies designate neoplasias of hematopoietic tissues, characterized by a disorder of the multiplication and differentiation of cells from one or more blood lines; Very few related studies are carried out in Africa due to diagnostic difficulties. We have carried out the present study to enrich the data on these pathologies. An analytical retrospective study was carried out in the hematology and medical oncology department of the Central Hospital of Yaoundé in Cameroon over 10 years, from January 1, 2008 to December 31, 2017. A technical sheet in which the epidemiological variables were noted, clinical, biological, therapeutic and evolutionary has been developed. Of the 167 files selected, the average age of the patients was 52 years +/- 16, with extremes of 21 and 87 years. Acute myeloid leukemias (AML) was more common in patients aged 45 to 54 (8 cases) and the disease affected more women than men at this age group (1H / 7F). Lymphoproliferative syndromes were the most common group of malignant hemopathies, accounting for 52.7% (88 patients). Non hodgkin lymphomas (NHL) were represented at all age groups with a male predominance. Patients with multiple myeloma clinically presented osteoarticular pain in 66.7% of cases. The chemotherapy protocols were varied according to the pathologies and their evolutionary stages. Toxic events were rare. Survival after one year was 9% for AML cases, 30% for CML cases. Few data being available on malignant hemopathies, this work allowed us to measure the importance of this group of pathologies in our context and to identify the clinical-biological profiles and the survival of the patients.

Keywords: Malignant hemopathies, Clinic, Treatment, Survival, Central Hospital of Yaoundé.

INTRODUCTION

Malignant hemopathies designate neoplasias of hematopoietic tissues, characterized by a disorder in the multiplication and differentiation of cells from one or more blood lines [1]. They contribute significantly to morbidity and mortality linked to cancer; it is the leading cause of death from cancer in the United States and the fifth most common cancer in the United Kingdom [2]. Due to diagnostic difficulties, there are not many studies carried out on these pathologies in Africa; in Cameroon, some recent studies are available but focused on the global characteristics of this group of diseases. It is with a view to enriching the data in Cameroon that the present study was conducted with the aim of describing the clinical-biological and progressive profile of each type of malignant hemopathy at the Central Hospital of Yaoundé.

MATERIAL AND METHOD

A retrospective study was conducted in the hematology and medical oncology department of the Central Hospital of Yaoundé (HCY) in Cameroon, which is the benchmark hospital for the care of adult patients with malignant hemopathies in the city of Yaoundé, the political capital of Cameroon.

An exhaustive consecutive sampling over 10 years, going from January 2008 to December 2017 was made. The medical records of patients followed in this service were included, in whom a diagnosis of malignant hemopathy had been made on the basis of cytological and / or histological examinations. The data were encoded and processed using Epi-Info 7 and Excel 2007 software. They were analyzed using SPSS 20 software. The quantitative variables were presented as mean and standard deviation (standard deviation) and the qualitative variables in numbers and percentages. Kaplan-Meier's survival analysis made it possible to determine the mean and median survival (with 95% confidence intervals) of the different delays of the participants during treatment.

RESULTS

We included 167 files with an average age of 52 years +/- 16 and extremes were 21 years and 87 years. The most represented age in frequency was 65 years were (22.2%) and the sex ratio was 1.6 in favour of males.

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Sociodemographic data

Acute myeloid leukemia (AML) was more common in patients aged 45 to 54 years and the disease affected more women than men in this age group (1M / 7W). Chronic lymphocytic leukemia (CLL) and chronic myeloid leukemia (CML) were mainly found in patients over 65 years of age (10 cases and 8 cases respectively) with a female predominance for CLL (3M / 7W) and male cases for cases of CML (7M / 1W). Non-Hodgkin's lymphoma (NHL) was represented in all age groups with a male predominance. Multiple myeloma (MM) was strongly represented in patients aged 55 to 64 years (10 cases) with a male predominance (1).

Table 1: Distribution of malignant hemopathies according to age and sex

	Type	**AML**	**CLL**	**CML**	**NHL**	**MM**	**Others**
	Gender	**(37)**	**(22)**	**(26)**	**(27)**	**(36)**	**(19)**
18-24	**W**	2	0	1	0	0	1
	M	2	0	0	2	0	2
25-34	**W**	3	0	0	1	0	0
	M	3	1	4	2	0	0
35-44	**W**	2	2	1	2	1	1
	M	4	0	1	4	2	2
45-54	**W**	7	2	1	1	2	1
	M	1	3	5	5	5	3
55-64	**W**	3	3	3	2	5	1
	M	4	1	2	5	10	1
>=65	**W**	2	7	1	1	4	4
	M	4	3	7	2	7	3

Table 2: Distribution of patients by type of malignant hemopathy nosological

Hemopathies	Nosological entities	**Number**	**Percentage**
Acute leukemia	LAM	37	22,2%
	LAL	13	7,8%
Sub total		**50**	**29,9%**
Lymphoproliferative Others syndromes	LMNH	27	16,2%
	LLC	22	13,2%
	LH	1	0,6%
	MM	36	21,6%
	LB	2	1,2%
Sub total		**88**	**52,7%**
Myeloproliferative syndromes	LMC	26	15,6%
	SM	1	0,6%
	PV	1	0,6%
	TE	1	0,6%
Sub total		**29**	**17,4%**
Total		**167**	**100%**

Table 3: Distribution of chemotherapy protocols according to the type of malignant hemopathy

Protocol	LAM (36)	LLC (22)	LMC (26)	LNH (27)	MM (37)	Others	Total
ABVD-MP	0	0	0	0	0	1	1
Aracytine	9	0	0	0	0	1	10
CHOP	0	0	0	7	0	1	8
COP	1	0	0	2	0	0	3
Chloraminophène	1	17	0	0	0	0	18
Imatinib	0	0	4	0	0	0	4
Hydroxy urea	1	0	12	0	0	0	13
MP	0	0	0	0	8	1	9
MP-THAL	0	0	1	0	21	0	22
R-CHOP	0	0	0	8	0	0	8
VAD	0	0	0	0	2	0	2
VCD	0	0	0	0	2	1	3
Other treatments	10	0	2	7	3	5	27
Total	22	17	19	24	36	10	128

Table 4: Distribu Fate of patients according to the type of malignant hemopathy tion

	AML (37)	CLL (22)	CML (26)	NHL (27)	MM (36)	Others	Total
Relapse	20	6	3	7	13	6	55
Lost to follow up	6	4	7	4	10	1	32
Deaths	23	13	14	16	11	16	93
Alive	6	8	6	5	15	2	42

Table 5: Symptom-diagnosis delay specific to each malignant hemopathy in days

Hemopathy	Average	95% sup	Médian	Inf	Sup
Others	220	390	47	25	69
LAM	180	289	96	80	112
LLC	173	292	88	50	126
LMC	130	199	103	50	156
LNH	312	535	144	59	229
MM	270	375	164	112	216

Table 6: Diagnosis-death delay speciffic to each malignant hemopathy in days

Hemopathies	Average	95% inf	95% sup	Médian	95% inf	95%s up
Autres	178	0	366	23	0	122
LAM	87	16	158	34	5	63
LLC	486	173	800	353	73	633
LMC	335	72	598	161	0	322
LNH	302	90	513	172	0	479
MM	712	383	1042	724	230	1218

History of surgery, alcoholism and high blood pressure was more prevalent in patients with MM, respectively 27.8%; 11.1% and 13.9% ; 75% of HIV infections were associated with NHL (Figure 1).

Agricultural pesticides and herbicides were more associated with NHL cases; benzene and paints were more linked to AML cases and exposure to hydrocarbons was more represented in cases of CML (Figure 2).

Frequency and clinical aspects

Lymphoproliferative syndromes were the most common group of malignant hemopathies, accounting for 52.7% (88 patients). The group of acute leukemias and myeloproliferative syndromes followed at respective proportions of 29.9% and 17.4%. These pathologies were distributed as in Table 2.

Patients consulted in the department mainly for "suspected malignant hemopathy" (89.2%) then for 5.4% anemia. 1.8% had asthenia, hyperleukocytosis, low back pain and deterioration in general condition; 1.8%; 1.2% and 0.6% of patients.

Patients with multiple myeloma clinically presented osteoarticular pain in 66.7% of cases. Anemic syndrome, AEG syndrome and hemorrhagic syndrome predominated in cases of AML (62.2%; 56.8% and 18.9%, respectively) (Figure 3).

Biological data

At the hemogram, anemia predominated in patients with multiple myeloma (85.3%). Hyperleukocytosis was strongly represented in lymphoproliferative syndrome with a peak for CLL (90.5%). Thrombocytopenia was highly represented, with peaks for AML (51.4%) and CLL (71.4%). Pancytopenia was found mainly in patients with AML (32.4%) (Figure 4).

Elevated uric acid levels were found in 100% of multiple myeloma and CLL.

Beta2 microglobulin was elevated in 100% of CLLs. LAM, CML, NHL, MM mainly had a high level of beta2microglobulins in the respective proportions of 66.7%; 66.7%; 81.8% and 75%.

Blood urea was normal in 56.3% of AML cases; 81.8% of CLL cases; 61.5% of CML cases; 66.7% of NHL cases; 43.5% of MM cases and 57.1% of the rest of the hemopathies.

Total protein was increased in 70.8% of MM cases; the rate was normal at 57.1% in AML cases and decreased to 57.1% in CLL cases.

The LDH level was high in 100% of the cases of LAM and LLC. 66.7% of NHL cases and 70% of MM cases also had an increased LDH. In 75% of CML a normal rate was observed.

For the diagnosis of CLL, all patients had performed immunophenotyping (100%). The evaluation of the MATUTES score in patients found that 81.5% had a score of 5 and 18.5% a score of 4.

Therapeutic data

The chemotherapy protocols used varied according to the type of pathology (Table 3):

- For cases of multiple myeloma, 22 patients out of 36 (61.1%) had received the Melphalan-Prednisone-Thalidomide protocol (MPT); 9 out of 36 patients or 25% of the cases were only on Melphalan + Prednisone (MP); The Vincristine- Cyclophosphamide - Dexamethasone (VCD) protocol was found at 8.3% (in 3 patients) and Vincristine - Adriblastine - Dexamethasone (VAD) at 5.5% (in 2 patients).

- Of CLL patients, 18 out of 22 (81.8%) were on Chlorambucil

- Hydoxyurea preceded taking GLIVEC (Imatinib mesylate) in cases of hyperleucocyte CML ; 50% of CML patients had received hydroxyurea while 15% had received Imatinib.

- In NHL cases, 29.6% of patients had received Cyclophosphamide-Doxorubicin -Vincristine-Prednisone (CHOP); Rituximab -CHOP was also found in 29.6% of patients and Cyclophosphamide-Vincristine-Prednisone (COP) in 11.1% of cases.

Evolving data

Of our sample, 93 patients died (55.7%) and 32 were lost to follow-up (19.1%). We found 42 patients were alive (25.1%). Specifically, AML cases relapsed and died much more (20 relapses and 23 deaths out of 64). The majority of those lost to follow-up were patients with MM and CML (10 and 7, respectively, lost to follow-up) (Table 4).

The diagnosis of NHL was made 312 days after the onset of symptoms; that of the MM was placed 270 days later; the LAM 180 days later; CLL 173 days later and CML 130 days later (Table 5).

On average 712 days separated the diagnosis and the occurrence of a death in the event of MM. This was 486 days for LLC cases; 335 days for CML cases; 302 days for NHL cases and 87 days for LAM cases (Table 6).

Survival

Survival after one year was 9% for AML cases, 30% for CML cases, 45% for NHL cases, 57% for CLL cases and 68% for MM cases. The other malignant hemopathies had an average survival rate of 20% after one year (Figure 4).

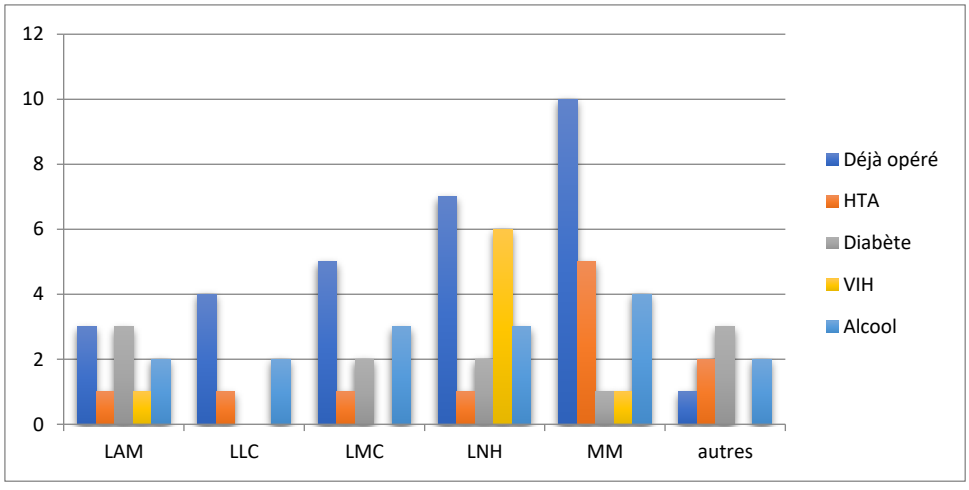

Figure 1: History according to the type of malignant hemopathy

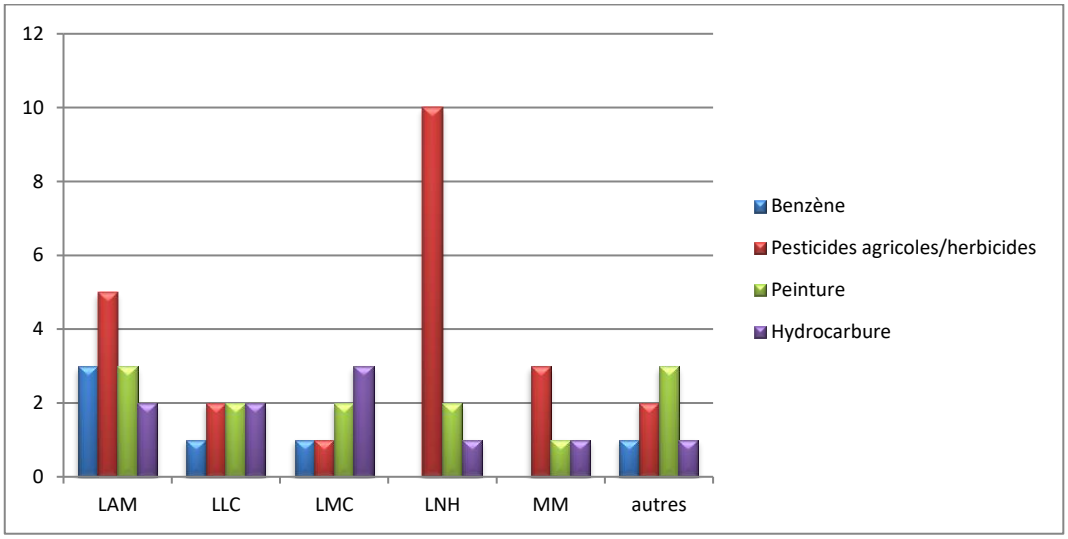

Figure 2: Exposure factors according to the type of malignant hemopathy

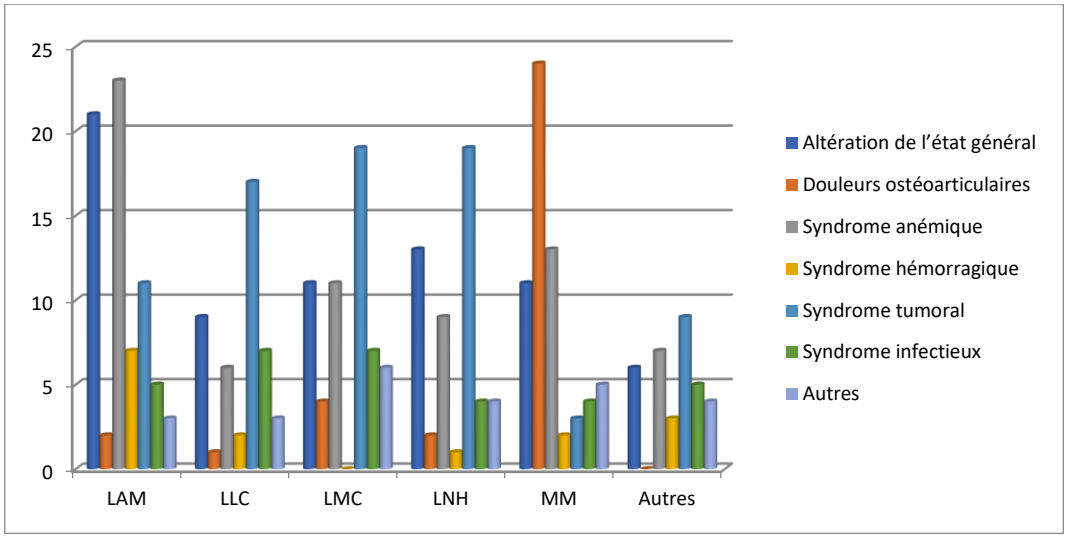

Figure 3: Clinical presentation according to the type of malignant hemopathy

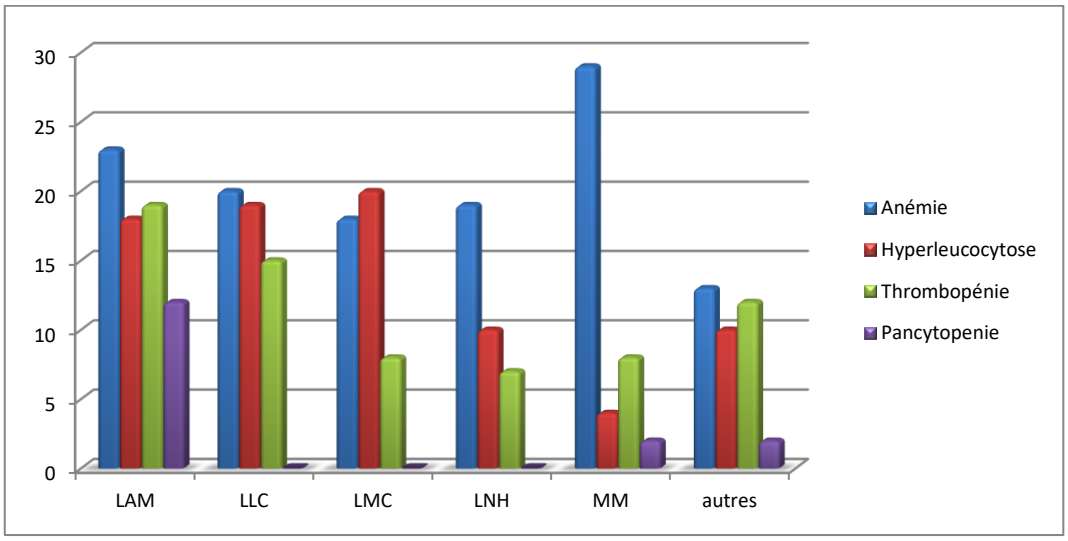

Figure 4: Finds at the NFS according to the type of malignant hemopathy

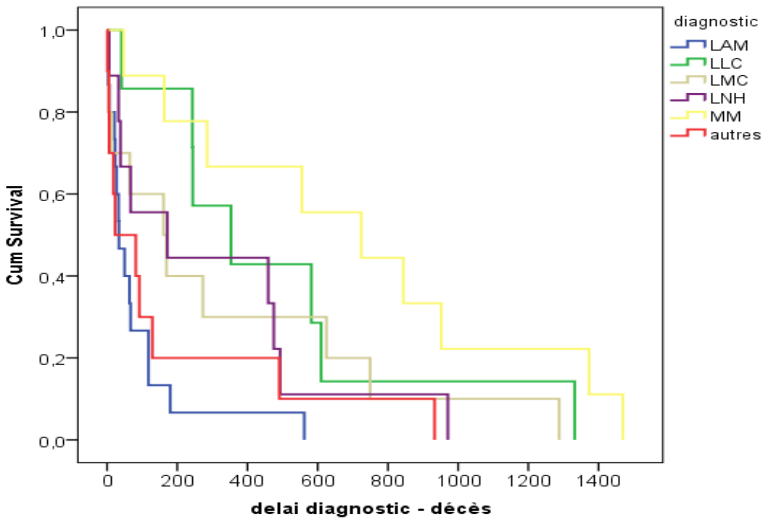

Figure 5: Kaplan Meier survival curve specific to each malignant hemopathy

DISCUSSION

Our study globally showed a male predominance in patients with hematologic malignancies with a sex ratio of 1.6. Other studies have also shown this male predominance [3-6]. Male superiority was mainly observed in MM and NHL. The leukemia group did not reproduce this difference much. "In low-resource settings, men are more likely to receive priority in receiving medical care"[7]. It is in this sense that Mohammad Sorowar Hossain and al. claimed that an underreporting of female cases could be explained by the socioeconomic situation of families [7]. The female predominance was especially in the cases of LAM and LLC in agreement with Atimere YN and al. in Abidjan who reported an unusual female predominance in leukemia cases [8].

In our study, the average age of our patients with malignant hemopathy was 52 years with extremes ranging from 21 to 87 years. This value is close to that of Ouedraogo and al. in Burkina Faso [9]. Indeed, they had found for patients aged over 15 years, an average age of 47.37 years. On the other hand, for extremes ranging from 2 to 90 years, Hossain MS. and al. in Bangladesh reported a lower average age of 42 years [7]; Luma and al. at the Douala General Hospital had extremes from 1 to 86 years with an average age of 45 years [4]. In Japan, China and India the average age was more between 65 and 70 years [10].

Also, during our study, it emerged that the frequency of HM increases with age. It was more marked in those over 65 years of age. We agree with Moustapha H. et al. in Sweden who shared with Dominique Bron et al. of the elderly hematology working group that patients with hematological malignancies are over 65 years of age [11,12]. This is likely due to the remarkably increased world life expectancy. Thus, current estimates suggest that the changes the largest in the world population over the next 40 years will be in the oldest age groups [13]. In our context, therapeutic progress over the years may also explain this result.

Patients with AML were mainly aged between 45 and 54 years (21.6%). This does not agree with the work of Mariam Doumbia et al. at Sina University Hospital which reported that the average age of AML patients was 9 years with extremes between 5 and 12 years for the vast majority of cases [14]. Mbanya et al. found a higher frequency of AML between 20 and 29 years of age [3]. This difference should be linked to the fact that their studies included both adults and children, yet ours only considers adult patients. Abraham-Jmiliet and al in Tunisia reported in 2009 that AML affected all ages between 2 months and 93 years with two frequency peaks between 10 and 20 years of age in young people and between 60 and 70 years of age in adults [3].

CLL and CML were found much more in subjects over the age of 65 (45.4% and 30.7% respectively). This data is in agreement with several reviews of literature [15,16] which stipulate that these diseases are frequent in the subject of the third age.

MM predominated between 55 and 64 years of age. This data corroborates with Seynabou Fall and al. in Senegal who reported an average age at diagnosis of 58.8 +/- 10 years with mainly subjects aged under 65 in 69.1% of the cases [17]. Slaheddine Chkir and al. in Tunisia rather reported a peak frequency of the disease at 70 years with a predominance in subjects aged over 65 years [18]. This difference is linked to life expectancy, which is higher in Tunisia.

The majority of patients were from the West Cameroon region (37.7% of cases). We agree with Luma et al. who reported a predominance of patients from the West among coastl malignant hemopathies (45.16%). This would be due to the high density of inhabitants from this region living in the Center and on the coast or the high exposure of these inhabitants to risk factors for malignant hemopathies, in particular exposure to agricultural pesticides and the volcanic environment.

Patients resided more often in urban areas (77.2%). This agrees with Steyn and al. in South Africa who reported true urban exposure to all chronic diseases in general and malignant hemopathies in particular: those who have spent most of their lives in urban areas tend to have more unhealthy lifestyles and higher risk of chronic diseases, of malignant hemopathies compared to their less urbanized counterparts [15,19]. This urban predominance of cases couldalso be due in our context to the under diagnosis of malignant hemopathies in rural areas probably because of the financial difficulties of the populations.

The patients for whom exposure was identified represented 31.1% of the total workforce, ie 52 patients. Agricultural pesticides and herbicides were by far the main exposure factors in 13.8% of cases. They were followed by paint, hydrocarbons and benzene respectively at 7.7%; 5.9% and 3.5%. We agree with the literature review and other studies which noted the action of these different exposure factors in the occurrence of malignant hemopathies [20,21]. In Douala, Luma et al. also reported high exposure to agricultural pesticides and herbicides (5.24%) [4].

In our study, a history of smoking was found in 3 patients (1.8%). This data is similar to that of Ngouadjeu et al. who counted only 6 patients (2.42%). Diallo DA and al. found 22 smoking patients [5]. Alcohol consumption was found in 16 patients (9.6%) unlike Luma et al. who found it in 38 patients (15.32%) [4].

The associated infectious diseases were HIV and HCV at 4.8% and 1.8% respectively. Our observation is similar to that of de Diop et al. in Senegal who reported in 2004 4.8% of HIV seropositivity on a sample of 107 patients [22]. It is also similar to that of Luma et al. who reported 5.65% of cases of HIV infection [4]. However, this value is lower than the 11.4% of HIV infection of Diallo Da et al. We therefore agree with Mbanya and al. that HIV infection may be a determining factor in the development of hematological malignancy [23]. We found that 75% of HIV infections were associated with NHL. Our observation is corroborated by the literature review which informs that: the incidence of NHL associated with HIV has considerably decreased but remains higher compared to HIV-negative people (10 times higher). Ghrabi and al. in Lyon reported that the majority of NHL patients (58%) had heterosexual transmission of HIV, 34% were intravenous drug users and 8% were gay men [24].

Patients with viral hepatitis C represented 1.8% of cases (3 cases); no cases of viral hepatitis B were noted. Our observations are lower than those of Luma et al. who reported 9 cases (3.63%) of HCV and 4 cases (1.61%) of HBV. Similarly, Diallo DA et al. in Mali reported 4 cases of HBV and 1 case of HCV in 2005 [4,5].

Regarding AML, 3 cases were observed in the diabetic field. However, we did not find any article, no literature review which would have hypothesized any link between these two chronic pathologies.

Out of 978 archive files corresponding to the 10 year period (2008-2017), were tained 167 files for our study. This gave us an average of 17 cases of malignant hemopathies per year. This data is much lower than that of N'dhatz and al. in Ivory Coast who had worked over a period of 9 years and reported 81 new cases of malignant hemopathies per year [25]. Thiam and al. in Dakar found 30 cases per year for a period of 6 years [26]; Luma and al. reported to the General Hospital of Douala 35 cases per year over a period of 7 years [4]; Diallo and al. had noted 33 cases per year over 6 years in Bamako [6]. The difference observed would be related to our smaller sample, limited to adults. The years 2016 and 2017 were the years with the highest number of cases : 31 and 43 cases respectively. We can therefore say, like other authors, that the number of malignant hemopathies diagnosed has increased over the years.

The most frequent hemopathies were developed at the expense of lymphoid tissue (60.48%). We agree with Luma and al. who reported a predominance of lymphoid hemopathies (67.34%). This observation was also noted by several other authors.

The most common hemopathy was AML (22.2%) followed by MM (21.6%), NHL (16.2%) and CML (15.6%). Numerous studies which present the group of leukemias as being the most frequent group of malignant hemopathies [20,15,27]. Mbanya et al. reported that the most common hemopathies were CML (27.2%), CLL (25.6%) and NHL, respectively (2.6%) [28].

Of our sample, 84.4% were referred. The majority of references were made by general practitioners (71.9%) and the minority by specialist physicians (12.6%). Direct consultation with the hematologist constituted the large minority of the mode of admission (5.4% of cases). We agree with Diallo DA and al. who reported that medical referrals made up the majority of admissions (69.3% of cases) [5]. This could be explained by the non popularization of the onco-hematological specialty especially in our context and the lack of knowledge by the general public of the problems it deals with.

In our series, the most frequent clinical presentation was tumor syndrome in 46.7% of cases. General impairment syndrome (42.5% of cases) and anemic syndrom (41.3% of cases) were as follows. Wea gree with literature reviews and numerous authors [5,15,29,30] including Luma et al. who reported mainly : 37% of tumor syndrome and 26.27% of anemic syndrome [4].

The most common assessment was the hemogram (95.2% of patients). Anemia was found in 76.7% of patients, followed by hyperleukocytosis and thrombocytopenia in 50.9% and 43.4% respectively. Hyperleukocytosis could be explained by the fact that it was accompanied by either a tumor syndrom or an anemic syndrom. An association of biological signs, namely: anemia, hyperleukocytosis and thrombocytopenia in agreement with the data in the literature had been observed in the series by Ouedraogo et al. in Burkina Faso, Luma et al. in the coast and Sawadogo et al. in Abidjan [4,9,31].

Pancytopenia was present in 10.1% of patients. This agrees with Atipo Tsiba and al. in Congo Brazzaville who reported that malignant hemopathies are one of the main etiologies of pancytopenia (38.75%) with acute leukemia in mind [32].

Anemia was increased in patients with multiple myeloma while hyperleukocytosis prevailed in lymphoproliferative syndrome with a peak in CLL. These results are in agreement with the literature review [15,33]. Luma et al. also reported the same conclusions as several other authors.

Thrombocytopenia was predominant (43.4%) as confirmed by other studies on malignant hemopathies [5,6,34].

From our study, we identified 128 patients (76.6%) who had received a chemotherapy protocol. This makes 1 in 4 patients who had not received cancer chemotherapy. This ratio is close to that of Diallo DA et al. who reported in Mali that 1 in 3 patients did not receive chemotherapy. This would be due to the high cost of this therapy [5].

Treatment-related complications were observed in 6.3% of patients and included: respiratory (3.1%), renal (1.6%), digestive (0.8%) and haematological (0.8%) toxicity . This is not supported by the results of Diallo DA et al. [5] who recorded many more toxic events (284) with priority liver, hematological, digestive and renal toxicity. This difference would be due to better monitoring of patients at home or to the loss of certain data resulting in poor filling of medical records

Of the 167 patients meeting the inclusion criteria, 93 had died, or 55.7% of the cases. These results are far superior to those of F.Z. Mahboub and al. in Casablanca, Morocco, who reported the death of 14 cases out of 132 (10.6%) from 1989 to 2014 [35]. E. Andres et al. in Strasbourg, France, there was a favorable development in more than 97% of malignant hemopathies (3 deaths out of 106) from 1990 to 2010 [27]. This would be due to earlier and standardized management in richer countries with patients who are quicker to meet the costs of treatment.

Those lost to follow-up represented 53.9% of cases. This data does not corroborate with that of F.Z.Mahboub in Morocco who reported only 8 cases of loss of sight or 6% of patients [34]. This difference could be due to the poverty of our patients who find it difficult to meet the costs of care unlike those of richer countries.

In our series, 55 patients had relapsed, or 32.9%. This is a figure that contrasts sharply with the findings of F.Z. Mahboub et al. who observed only 8 cases of relapse, ie 6% [34]. The high rate in ourcontext of these relapse cases would be due to the non-standardization of the various protocols of care in our patients and probably to financial limits.

However, 42 patients were still alive and on management protocol. This figure represents much less than half of our sample: 25.1% of cases. On the other hand, in Morocco F.Z. Mahboub and al. reported remission in 69 cases and 20 live cases still in treatment [34]. The survival rate was evaluated at 30% in 1 year for all malignant hemopathies and at 1% in 4 years. This agrees with Siné Bayo and al. who reported to the Point G Hospital in Bamako 65% of deaths in the year following the diagnosis and a longer survival which did not exceed 4 years in patients suffering from malignant hemopathies [34].

CONCLUSION

In the light of this retrospective work over 10 years, it emerges that the problem of malignant hemopathies is serious and worrying. The prognosis despite an improvement in recent years remains generally grim. Good prevention requires special attention from groups at risk, concrete actions aimed at reducing risk factors and strengthening protective factors, in particular environmental protection.

Conflicts of Interest

The authors declare no conflicts of interest.

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