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Hematologic malignancies in children: Epidemiological aspects in the pediatric oncology department of Oran Anti-Cancerous center, Algeria (2009-2013)

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ABSTRACT

The incidence of the hematological malignacies, cancers of blood and lymphoid organs, has been in continuous increase for the last 20 years. In Algeria, few data on hematologic malignancies are available in the absence of a population register. The aim of this work is to describe the epidemiological aspect of hematologic malignancies in children from northwestern Algeria.

This study was carried out in 366 patients, with hematological malignancies, aged from 1 month to 15 years, over a period of 5 years (2009-2013). The study was carried out in the Anti-Cancerous Centre of Oran, Algeria.

We noted a predominance of male gender comparing to the females with a sex ratio M/F of 1.2. A male predominance was found for all pathologies (sex ratio of 1.08 for acute lymphoid leukemia, ALL) except for acute myeloid leukemia, AML where a female predominance was observed with a sex ratio F/M of 1.21. 0-3 years age group is the most affected by these haemopathies with 34.2%, however, patients older than 10 years are the least affected. The most frequent malignant haemopathies was the ALL with 60.9%, followed by the AML with 16.9%. The mortality rate in all the studied patients is about 8.2%. The mortality rate in patients with chronic myeloid leukemia (CML) was about 20%, which is significantly higher compared to those recorded in patients with ALL and LH (5.4% and 5%, respectively).

This study highlights the need for broader strategies for better understanding of all epidemiological aspects of childhood hematological malignancies and for adopting case management and prevention policies.

Keywords: Hematologic malignancies, epidemiological characteristics, children, acute lymphoblastic leukemia, Oran anti cancerous centre.

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INTRODUCTION

Hematological malignancies, neoplasms account for about 40% of cancers in children under the age of 15 years, and developed from the bone marrow hematopoietic cells and lymphatic system. This kind of hematological malignancy develops at the expense of lymphoid lines precursors, with a strong preponderance of B-lymphoid line.[1]

Leukemia is the most prevalent pediatric cancer. The acute lymphoid leukemia (ALL) accounts for about 80% of the cases (75% of them are B-ALL), whereas the acute myeloid leukemia (AML), which is traditionally encountered in adults, accounts for only 20% of cases.[2] Usually, the chronic lymphoid leukemia (CLL) is not found in children, however, the chronic myeloid leukemia (CML) is extremely rare.[3-4] The upsurge of Hodgkin's lymphoma (HL) incidence is associated with the age of children.[5] On the other hand, the non-Hodgkin's lymphoma (NHL) is very rare before the first year of life. The Burkitt lymphomas involving mature B-cells represent the half of the NHL and represent the most common histological type in children aged 3 to 8 years; nonetheless, their impact decreases in older children. The T and B lymphoblastic lymphomas represent 17% and 5% of cases, respectively.[6]

The ionizing radiation exposure is recognized as the major risk factor for malignant hemopathies in children[7]. However, other risk factors are established, such as non-ionizing radiation, electromagnetic fields of extremely low frequency and exposure to radon.[8-9]

The purpose of our retrospective study was to describe the epidemiological aspect of malignant hemopathies over a period of 5 years (2009-2013) at the level of pediatric oncology facility of the Anti-Cancer Centre of Oran (North-Western Algeria).

METHODS

In this descriptive retrospective study, we selected and treated the medical records of all patients, of both genders and aged from one month to 15 years, admitted to the hematological clinic or hospitalized at the pediatric oncology department of the Anti-Cancer Centre of Oran (North-Western Algeria) over a period of five years (2009-2013). The inclusion criteria were based on a positive diagnosis of malignant homeopathy after cytological and/or histological examination. However, clinical hematological manifestations and therapeutic aspects were excluded.

Data were processed and analyzed by SPSS software version 22.0 ('Statistical package for Social Sciences', IBM Corporation, Chicago, IL August 2013) for Windows. For all analyzes, a *p*-value of 0.05 or less was considered significant with a confidence interval of 95%. The Chi-square test was used to compare the values expressed in frequency (%). The relationships between the different parameters were studied using Pearson's correlation test and the simple linear regression test with a 95% confidence interval (CI 95%).

RESULTS

A total of three hundred sixty-six (366) patients, aged from one month to 15 years, were enrolled in this retrospective study. We noted a predominance of male gender comparing to the females (54.6% *vs.* 45.4%, respectively) (Table 1), with a sex ratio M/F of 1.2.

As described in figure 1, male predominance was found for all pathologies (e.g. sex ratio M/F of 1.08 for ALL) except for acute myeloid leukemia (AML) where a female predominance was observed (34 girls against 28 boys with a sex ratio F/M of 1.21).

The mean age of all participants was 6.39±4.33 years (76.72± 52.05 month) (Table 2). The highest prevalence of the studied pathologies was recorded in the age group of 0-3 years with 34.2%, followed by the age group of 4-6 years with 24.3%. However, the prevalence in the age groups of 10-12 and 13-15 years was 12.0% and 13.9%, respectively. The majority of malignant hemopathies were observed before the age of 3 years (38.1% of ALL). Though, the frequency of HL increases in children after the age of 4 years (Table 3) and (Figure 2).

The most frequent malignant hemopathies was the ALLs with 60.9%, followed by the AML with 16.9%. In contrariwise, low prevalence was observed of CML and NHL with 2.7% and 8.5%, respectively (Table 4).

Using the Pearson correlation test, positive no significant association was noted (r^2=0.006, p=0.139) between the age of children and the type of pathology (Table 5 and 6).

As illustrated in table 7, the annual incidence of malignant hemopathies has steadily increased in Oran from 68 cases in 2009 to 96 cases in 2012. Although, a decrease in the ALLs was observed (from 56 cases in 2009 to 35 cases in 2012) (Figure 3).

As summarized in Table 8 and 9, high significant correlation (r^2=0.091, p<0.001) was observed between the type of pathology and the years of hospitalization of patients.

Results from our study disclosed a mortality rate of 8.2% in the studied population (Table 10). The mortality rate was fairly high in patients with AML and CML, with 16.1% and 20%, respectively. On the other hand, low rates were noted in patients with ALL and HL with 5.4% and 5%, respectively (Table 11) and (Figure 4).

As depicted in Table 12 and 13, no significant correlation (r^2=0.008, p=0.073) was observed between the number of deaths and the type of pathology.

Table 1: Distribution of patients by gender

		Effective	Percentage%	Valid Percentage	Cumulative Percentage
Valid	F	166	45.4	45.4	45.4
	M	200	54.6	54.6	100.0
	Total	366	100.0	100.0	

Table 2: Distribution of patients by age (by years and months)

	N	Minimum	Maximum	Median	Variance	Average	Standard Deviation
Age (year)	366	0.083	15.000	6.00	18.819	6.39367	4.338128
Age (month)	366	1.00	180.00	72.00	2709.988	76.7240	52.05754
N valid (listwise)	366						

Table 3: Distribution of pathologies by ageof patients

			Type of pathology					Total
			ALL	AML	HL	CML	NHL	
Age range (years)	Less than 3 years	Effective	85	19	7	3	11	125
		% included in age range (years)	68,0%	15,2%	5,6%	2,4%	8,8%	100,0%
		% included in type of pathology	38,1%	30,6%	17,5%	30,0%	35,5%	34,2%
	4 to 6 years	Effective	51	17	12	5	4	89
		% included in age range (years)	57,3%	19,1%	13,5%	5,6%	4,5%	100,0%
		% included in type of pathology	22,9%	27,4%	30,0%	50,0%	12,9%	24,3%
	7 to 9 years	Effective	36	6	9	1	5	57
		% included in age range (years)	63,2%	10,5%	15,8%	1,8%	8,8%	100,0%
		% included in type of pathology	16,1%	9,7%	22,5%	10,0%	16,1%	15,6%
	10 to 12 years	Effective	23	10	5	0	6	44
		% included in age range (years)	52,3%	22,7%	11,4%	0,0%	13,6%	100,0%
		% included in type of pathology	10,3%	16,1%	12,5%	0,0%	19,4%	12,0%
	13 years and more	Effective	28	10	7	1	5	51
		% included in age range (years)	54,9%	19,6%	13,7%	2,0%	9,8%	100,0%
		% included in type of pathology	12,6%	16,1%	17,5%	10,0%	16,1%	13,9%
Total		Effective	223	62	40	10	31	366
		% included in age range (years)	60,9%	16,9%	10,9%	2,7%	8,5%	100,0%
		% included in type of pathology	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%

Table 4: Distribution of patients by the type of pathology

		Effective	Percentage%	Valid Percentage	Cumulative Percentage
Valid	ALL	223	60.9	60.9	60.9
	AML	62	16.9	16.9	77.9
	HL	40	10.9	10.9	88.8
	CML	10	2.7	2.7	91.5
	NHL	31	8.5	8.5	100.0
	Total	366	100.0	100.0	

Table 5: Relationship between type of pathology and age

Correlations (Coefficient of correlation r=0.077)			
		Type of pathology	Age Group (years)
Correlation of Pearson	Type of pathology	1.000	0.077
	age range (years)	0.077	1.000
Sig. (unilateral)	Type of pathology	.	0.070
	age range (years)	0.070	.
N	Type of pathology	366	366
	age range (years)	366	366

Table 6: Meaning test (Fisher Report)

ANOVA[a] (Fisher test F=2.198, *p*=0.139)						
Model		Sum of squares	dOF	Average of squares	D	Sig.
1	Regression	3.412	1	3.412	2.198	0.139[b]
	Residue	565.200	364	1.553		
	Total	568.612	365			
a. dependent Variable : Type ofpathology						
b. predicted Values : (constants), age range (years)						

Table 7: Distribution of pathologies by year of recruitment of patients (incidence)

			Type of pathology					Total
			ALL	AML	HL	LMC	NHL	
year	2009	Effective	56	10	0	0	2	68
		% included in year	82,4%	14,7%	0,0%	0,0%	2,9%	100,0%
		% included in type of pathology	25,1%	16,1%	0,0%	0,0%	6,5%	18,6%
	2010	Effective	49	8	1	2	0	60
		% included in year	81,7%	13,3%	1,7%	3,3%	0,0%	100,0%
		% included in type of pathology	22,0%	12,9%	2,5%	20,0%	0,0%	16,4%
	2011	Effective	44	13	3	3	5	68
		% included in year	64,7%	19,1%	4,4%	4,4%	7,4%	100,0%
		% included in type of pathology	19,7%	21,0%	7,5%	30,0%	16,1%	18,6%
	2012	Effective	35	17	23	2	19	96
		% included in year	36,5%	17,7%	24,0%	2,1%	19,8%	100,0%
		% included in type of pathology	15,7%	27,4%	57,5%	20,0%	61,3%	26,2%
	2013	Effective	39	14	13	3	5	74
		% included in year	52,7%	18,9%	17,6%	4,1%	6,8%	100,0%
		% included in type of pathology	17,5%	22,6%	32,5%	30,0%	16,1%	20,2%
Total		Effective	223	62	40	10	31	366
		% included in year	60,9%	16,9%	10,9%	2,7%	8,5%	100,0%
		% included in type of pathology	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%

Table 8: Relationship between type of pathology and year of recruitment

Correlation (Coefficient of correlation r=0.301)			
		Type of pathology	Year
Correlation of Pearson	Type of pathology	1.000	0.301
	Year	0.301	1.000
Sig. (unilateral)	Type of pathology	.	0.000
	Year	0.000	.
N	Type of pathology	366	366
	Year	366	366

Table 9: Meaning test (Fisher Report)

ANOVA[a](Fisher report F=36.221, $p<0.001$)						
Model		Sum of squares	dOF	Average squares	F	Sig.
1	Regression	51.460	1	51.460	36.221	0.000[b]
	Residue	517.152	364	1.421		
	Total	568.612	365			
a. dependent Variable : Type of pathology						
b. predicted Values : (constants), Year						

Tableau 10 : Mortality rate in patients with haematological malignancies

		Effective	Percentage%	valid Percentage	cumulative Percentage
Valid	*deceased*	30	8.2	8.2	8.2
	not deceased	336	91.8	91.8	100.0
	Total	366	100.0	100.0	

Table 11: Mortality rate for all haematological malignancies

			Type of pathology					Total
			ALL	AML	HL	CML	NHL	
Death	DCD	Effective	12	10	2	2	4	30
		% included in Death	40,0%	33,3%	6,7%	6,7%	13,3%	100,0%
		% includedinType of pathology	5,4%	16,1%	5,0%	20,0%	12,9%	8,2%
	NDC	Effective	211	52	38	8	27	336
		% included in Death	62,8%	15,5%	11,3%	2,4%	8,0%	100,0%
		% included inType of pathology	94,6%	83,9%	95,0%	80,0%	87,1%	91,8%
Total		Effective	223	62	40	10	31	366
		% included in Death	60,9%	16,9%	10,9%	2,7%	8,5%	100,0%
		% included inType of pathology	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%

Table 12: Relationship between mortality and type of pathology

Correlation (Coefficient of correlation r=-0.094)

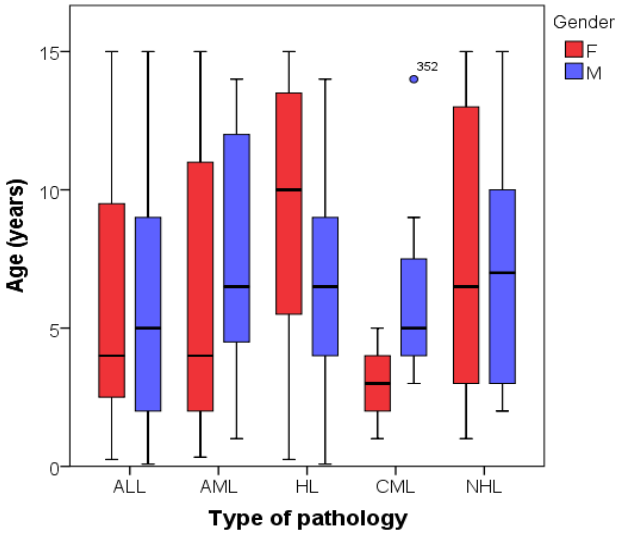
		Death	Type ofpathology
Correlation of Pearson	Death	1.000	-.094
	Type of pathology	-.094	1.000
Sig. (unilateral)	Death	.	0.037
	Type of pathology	0.037	.
N	Death	366	366
	Type of pathology	366	366

Tableau 13: Meaning test (Fisher Report)

ANOVA[a](Fisher test F=3.231, *p*=0.073)

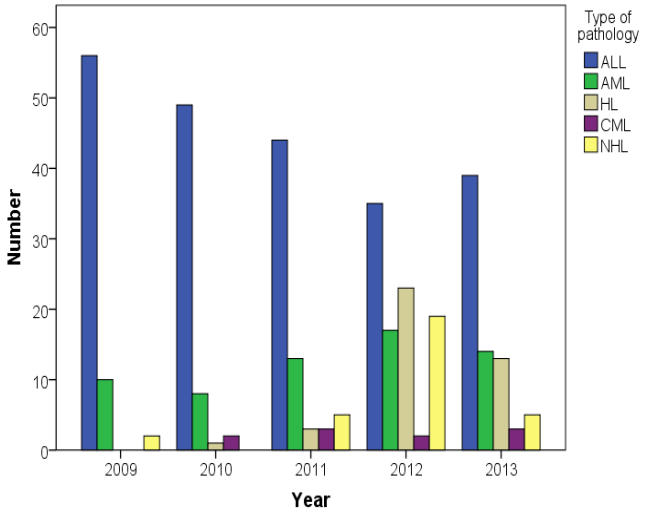
Model		Sum of squares	dOF	Average squares	F	Sig.
1	Regression	0.242	1	0.242	3.231	0.073[b]
	Residue	27.299	364	0.075		
	Total	27.541	365			

a. Dependent variable : Death b. Predicted values: (constant), Type of pathology



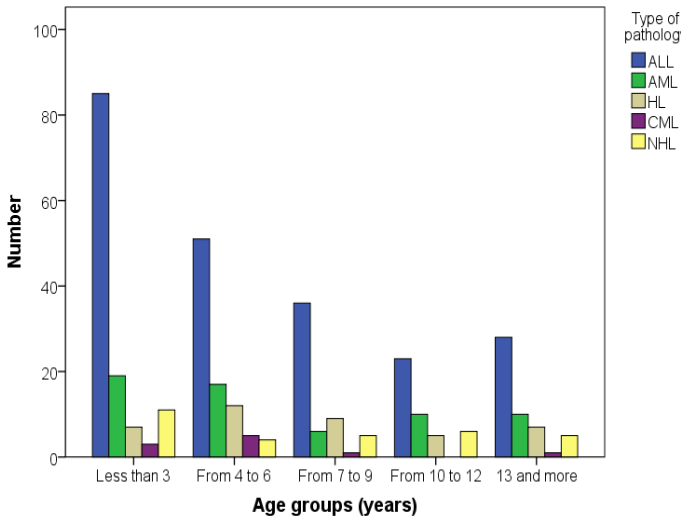
ALL: Acute Leukemia Lymphoid **AML:** Acute Myeloid Leukemia
HL: Hodgkin's lymphoma **CML:** Chronic Myeloid Leukemia
NHL: Non-Hodgkin's lymphoma

Figure 1: Average age of patients by type of pathology and gender



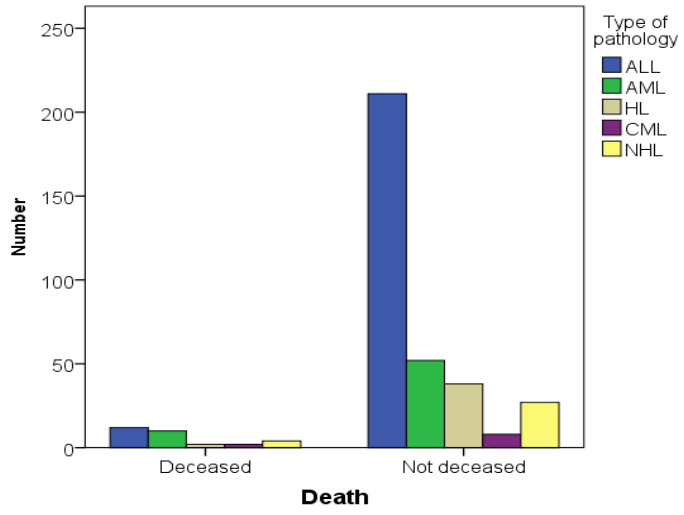
ALL: Acute Leukemia Lymphoid **AML:** Acute Myeloid Leukemia
HL: Hodgkin's lymphoma **CML:** Chronic Myeloid Leukemia
NHL: Non-Hodgkin's lymphoma

Figure 3: Distribution of pathologies according to the year of recruitment



ALL: Acute Leukemia Lymphoid **AML:** Acute Myeloid Leukemia
HL: Hodgkin's lymphoma **CML:** Chronic Myeloid Leukemia
NHL: Non-Hodgkin's lymphoma

Figure 2: Distribution of pathologies according to the age of patients



ALL: Acute Leukemia Lymphoid **AML:** Acute Myeloid Leukemia
HL: Hodgkin's lymphoma **CML:** Chronic Myeloid Leukemia
NHL: Non-Hodgkin's lymphoma

Figure 4: Mortality rates for all haematological malignancies

DISCUSSION

In this retrospective epidemiological study, we aimed to describe the epidemiological aspect of malignant hemopathies in children aged 1 month to 15 years. The study was carried out over a period of 5 years (2009-2013) at the level of the pediatric oncology facility of the Anti-Cancer Centre of Oran (North-Western Algeria). To the best of our knowledge, this investigation is the first to describe the malignant hemopathies characteristics in this health facility. The outcomes of the current study revealed an increased incidence of the malignant hemopathies during the last decade in the Northwestern region of Algeria (*Wilaya* of Oran). Similar conclusions were reported from two studies carried out in Abidjan between 1995 and 2004 and from the United States.[10, 11] Likewise, an upsurge in the incidence of these pathologies has been shown by the European data of ACCIS (Automated Childhood Cancer Information System).[12]

The sex ratio M/F in our study was 1.2. This finding matches the results obtained in France by Desandes *et al.* in 2004 (sex ratio M/F between 1 and 1.4).[13] Similarly, Lahlou *et al.* in Morocco reported a male gender predominance in ALL patients with a higher sex ratio (1.32).[14] Several authors highlighted the higher prevalence of AML in male subjects, which is inconsistent with the results of our study. [15-16] The association between the female gender and the risk of AML must be further explored in order to better understand this complication.

Malignant hemopathies represent about 40% of all cancers before the age of 15 years. 34.2% of malignant hemopathies were observed before the age of 3 years, these findings are in agreement with the results of a European study carried out by Clavel *et al.* where a higher incidence of malignant hemopathies was recorded in children under 5 years of age during.[16] According to *Goubin et al.,* 80% of cases of childhood leukemia are acute lymphoblastic leukemia (ALL). This complication could occur at any age, and more particularly between the 1st and 10th years of life. The higher incidence has been reported between 2 and 3 years.[17] In our study, the highest incidence was observed between 0-3 years. The incidence of acute myeloid leukemia (AML) is higher in children less than 3 years of age and then decreases markedly. This decrease can be explained by the fact that LAM is more frequent in adults.[18] Few cases of Hodgkin's lymphoma (HL) were noted in our studied population before the age of 4 years, this could be explained by the fact that this disease increases with age.[19] Chronic lymphocytic leukemia (CLL) is not found in children and chronic myeloid leukemia (CML) are extremely rare, as these two pathologies mainly affect the elderly.[20, 21]

Some studies have been devoted to evaluate the malignant hemopathies' mortality in Algeria and Africa. Despite the improved diagnosis and therapeutic progress made during the last few decades, malignant hemopathies' mortality remains relatively high. In the area of Sidi-Bel-Abbes (North-Western Algeria), the mortality rate was about 8.2%. This frequency might be explained by the lack of diagnostic tools at the hematology department and the consultation delays. However, any disease prognosis depends on the precocity and the accessibility to medical care. One limitation of the present study is the retrospective aspect that does not allow optimizing the collection of some information in when medical records are not standardized.

CONCLUSION

The childhood malignant homeopathies have particular epidemiological characteristics in the region of Oran (North-Western Algeria). Our results highlighted a mortality rate that remains not negligible. More strategies involving further aspects and policies and based on patient information, public awareness and training of medical personnel are needed to help reduce the consultation time and better managing and preventing malignant homeopathies.

Conflicts of interest: There are no conflicts of interest.

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