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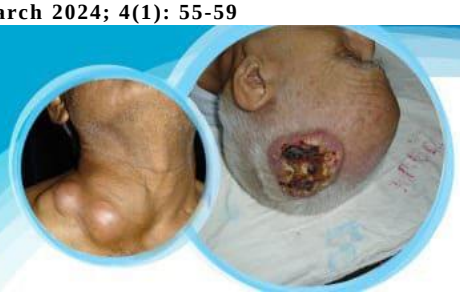

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Clinico-epidemiological study of hematological malignancies at clinical oncology department Tanta university hospitals

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Abstract
Background: Hematological malignancies (HMs) comprise a heterogeneous collection of malignancies, all originating from the bone marrow and lymphatic system. This study sought to characterize the clinical characteristics of HMs and ascertain the course of diffuse large B lymphoma as a common hematological malignancy with the aforementioned features.
Methods: This clinico-epidemiological study was conducted in 600 patients aged 18 years and older of both sexes with a histopathological or clinical history of HM. All patients underwent complete history, clinical examination, laboratory and radiological examination**.**
Results: The mortality rate was in 133 (24.77%) patients with mean value (95% CI) of 58.556 (56.33 - 60.77). Regarding disease-free survival (DFs), relapse occurred in 120 (20.00%) patients with mean value (95% CI) of 74.185 (71.665 - 76.705). The diagnosis of acute myeloid leukemia increased from 0.65% in 2016 to 0.88% in 2018 with no diagnosis of AML in 2019 and 2020. Chronic myeloid leukemia diagnosis increased from 1.95 in 2016 to 2.44% in 2020. The MM diagnosis increased from 24.68% in 2016 to 39.02% in 2020. The diagnosis of Hodgkin Lymphoma (HL), and Non-Hodgkin Lymphoma/ diffuse large B-cell lymphoma decreased from 5.58% and 53.9% respectively in 2016 to 12.2% and 39.02% respectively in 2020. Lost follow up occurred in 70 (11.67%) patients. Mortality occurred in 133 (22.17%) patients.
Conclusions: Long-term survival data associated with current treatment regimens have led to careful consideration of potential risk factors beyond 5 years.

Keywords: Epidemiology, hematological malignancies, Tanta university hospitals, Non-Hodgkin lymphoma, chemotherapy

Introduction

Haematological malignancies (HMs) comprise a heterogeneous collection of malignancies arising in the bone marrow and lymphatic system. There are three main groups: leukemia, lymphoma, and plasma cell neoplasms. Greater developed countries often have greater rates of leukaemia and lymphoma. Multiple leukemias and lymphomas are rare, and the specific etiology remains unclear. Evidence varies by type; survival rates are poor in acute leukemia in adults and good outcomes in Hodgkin lymphoma. There is an urgent need to improve access to testing and treatment services worldwide [1].

The latest GLOBOCAN estimate for non-Hodgkin lymphoma (NHL) predicts/estimates 509,590 NHL cases and 248,724 NHL deaths worldwide in 2018 [2].

NHL has historically been classified as indolent or acute based on its typical clinical course, although many patients are variable. Lemon comprises marginal B-cell lymphoma, low-grade lymphoma, and chronic lymphocytic leukemia/small cell lymphoma (CLL/SLL). Diffuse large B-cell lymphoma (DLBCL) and high-grade lymphoma are examples of lymphoma targets. Precursor B and T lymphoblastic leukemia/lymphoma, as well as Burkitt lymphoma (BL), are typically quite aggressive [3].

About Hodgkin Lymphoma (HL) in 2018, there were approximately, there are 26,167 cancer deaths and 79,990 cancer diagnoses globally [2].

According to GLOBOCAN estimates, the number of new HL cases worldwide has decreased by 6.1% when population growth and changing age patterns are considered [4].

The disease is more common in whites than in other races. The age distribution of HL is obviously bimodal, with young individuals (20-24 years old) having the highest prevalence and elderly persons (75-79 years old) having the lowest incidence [5].

The Middle East Cancer Centre in Egypt reports that the age-standardized incidence of NHL in children is 16.3/100,000. According to the National Cancer Institute (NCI), NHL accounts for 10.9% of all malignancies recorded annually in Egypt [6], making it the second most prevalent cancer in women and the third most common cancer in males due to this aggressive illness.

This study aimed to characterize the clinical characteristics of HMs and investigate the relationship between prognostic markers and the fate of large B-cell lymphoma, the most prevalent hematological malignancy.

Patients and Methods

This hospital-based clinical-epidemiological study was conducted in 600 patients aged 18 years and older of both sexes with histopathological and clinical history of HM. The study was conducted from January 2016 to December 2020 following clearance from Tanta University Hospital's ethics committee in Tanta, Egypt. The patients gave their informed permission.

Exclusion criteria were related to patients with stage II rather than HM and were not included in the statistical analysis. All patients underwent a complete history, physical examination [general examination included general appearance, vital signs, examination of the head and neck, chest, upper and lower body, and examination of the abdomen and pelvis (liver, kidney), and local examination including examination of the lymph nodes (occipital examination). , superficial cervical, supraclavicular, axillary, and pelvic)], laboratory examinations [complete blood count (CBC), renal and liver function tests, markers, histopathological markers, immunophenotyping, bone marrow and bone biopsy], and radiological examinations [computed tomography (CT), magnetic resonance imaging (MRI), ultrasound, positron emission tomography/CT (PET CT), and echocardiography.

Lines of treatment

Chemotherapy, radiotherapy, chemoradiotherapy, target therapy and surgery.

Evaluation and follow-up

The following information was collected from the medical literature. Response to treatment includes complete remission (CR) and progressive disease. Survival data express: overall survival (OS) and disease-free survival (DFs). Radiological evaluation included CT. Every 3 rounds of chemotherapy. After completion of chemotherapy, all patients underwent CT follow-up every 6 months for the first 2 years and annually thereafter. The time and location of relapse (proximal, regional,or more distant) were recorded for each patient. Patients who experienced local or distant treatment failure were evaluated clinically, radiologically (CT) and histopathologically “as indicated” to determine the location of treatment failure.

Statistical analysis

The statistical study was carried out with IBM Inc.'s SPSS v26 in Chicago, IL, USA. With the use of the Student's t-test, quantitative changes were compared between two groups and reported as mean and standard deviation (SD). The frequency and percentage (%) of the qualitative variables were reported, and where needed, the Fisher exact test or Chi-square test was used for analysis. The Kaplan-Meier curve was employed to illustrate the rates of death and recurrence. A strong number was defined as a two-sided P value less than 0.05.

Results

Seven hundred individuals were eligible, 70 were ineligible, and 30 refused to participate in our investigation. The remaining 600 patients were split into three cohorts. All eligible patients were followed up and statistically analysed.

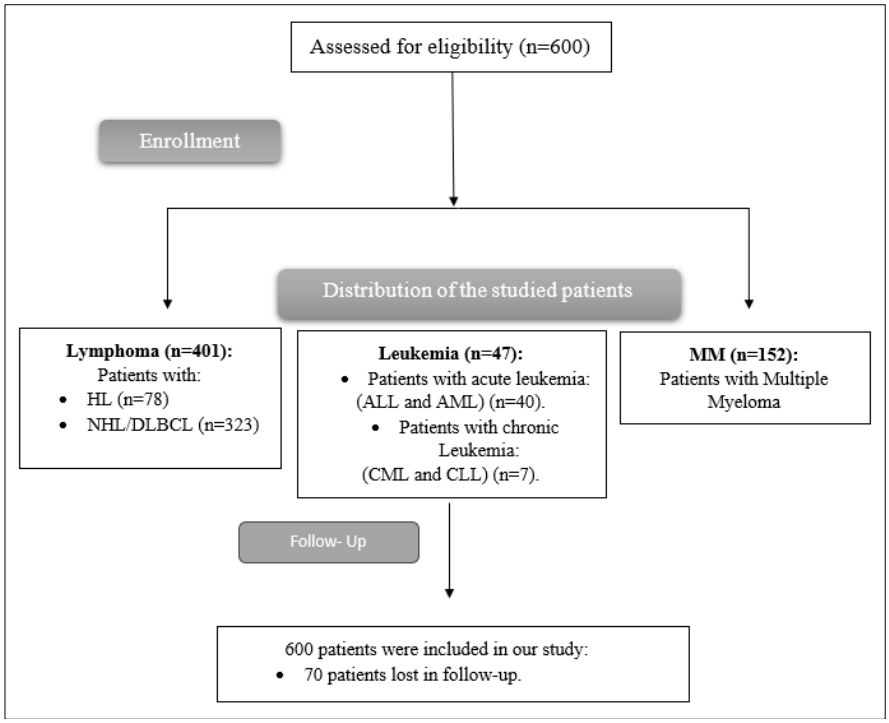


Fig 1: CONSORT flowchart of the enrolled patients

The mean of age was 52.19±15.2 years. Regarding sex, 322 (53.67%) patients were males, and 278 (46.33%) patients were females. Regarding Co-morbidities, 194 (32.33%) patients had DM, 105 (17.5%) patients, 171 (28.5%) patients had DM and HTN and 34 (5.67%) patients had cardiac disease. Regarding Special habits, 244 (40.67%) patients were smokers. Regarding diagnosis, ALL was present in 36 (6%) patients, AML in 4 (0.67%) patients, CML in 6 (1%) patients, CLL in 1 (0.17%) patient, HL in 78 (13%) patients, MM in 152 (25.33%) patients and NHL/DLBCL in 323 (53.83%) patients. Table 1.

Table 1: Demographic data and diagnosis of the studied patients

		N=600
Age (years)		52.2±15.2
Sex	Male	322 (53.67%)
	Female	278 (46.33%)
Co-morbidities	DM	194 (32.33%)
	HTN	105 (17.5%)
	DM and HTN	171 (28.5%)
	Cardiac disease	34 (5.67%)
	None	96 (16%)
Diagnosis	ALL	36 (6%)
	AML	4 (0.67%)
	CML	6 (1%)
	CLL	1 (0.17%)
	HL	78 (13%)
	MM	152 (25.33%)
	NHL/DLBCL	323 (53.83%)

Data are presented as mean ± SD or frequency (%). DM: Diabetes mellitus, HTN: Hypertension, ALL: Acute lymphocytic leukemia, AML: Acute myelogenous leukemia, CML: Chronic myelogenous leukemia, CLL: Chronic lymphocytic leukemia, HL: Hodgkin Lymphoma, MM: Multiple Myeloma, NHL: Non-Hodgkin Lymphoma, DLBCL: diffuse large B-cell lymphoma.

Diagnosis of the studied patients over the period (2016-2020) were enumerated in this table. Table 2.

Table 2: Diagnosis of the studied patients over the period (2016-2020)

	2016	2017	2018	2019	2020
ALL	5 (3.25%)	15 (6.3%)	7 (6.14%)	6 (11.32%)	3 (7.32%)
AML	1 (0.65%)	2 (0.84%)	1 (0.88%)	0 (0%)	0 (0%)
CML	3 (1.95%)	1 (0.42%)	1 (0.88%)	0 (0%)	1 (2.44%)
CLL	0 (0%)	1 (0.42%)	0 (0%)	0 (0%)	0 (0%)
HL	24 (15.58%)	32 (13.45%)	12 (10.53%)	5 (9.43%)	5 (12.2%)
MM	38 (24.68%)	62 (26.05%)	19 (16.67%)	17(32.08%)	16 (39.02%)
NHL/DLBCL	83 (53.9%)	125(52.52%)	74(64.91%)	25(47.17%)	16(39.02%)

Data are presented as frequency (%). ALL: Acute lymphocytic leukemia, AML: Acute myelogenous leukemia, CML: Chronic myelogenous leukemia, CLL: Chronic lymphocytic leukemia, HL: Hodgkin Lymphoma, MM: Multiple Myeloma, NHL: Non-Hodgkin Lymphoma, DLBCL: diffuse large B-cell lymphoma.

Chemotherapy and radiotherapy were enumerated in this table. Table 3.

Table 3: Chemotherapy and radiotherapy of the studied patients

			N=600
Chemotherapy			255 (42.5%)
Type of chemotherapy and target	NHL	CHOP	81 (13.5%)
		R-CHOP	40 (6.67%)
		CVP	54 (9%)
	MM	VAD	18 (3%)
		VAD and Vilcade	17 (2.83%)
		VAD + Zometa	15 (2.5%)
	HL	ABVD	30 (5%)
Radiotherapy			419 (69.83%)
Radiotherapy details	Breast irradiation		2 (0.33%)
	Cervical & axillary irradiation		84 (14%)
	Whole brain irradiation		76 (12.67%)
	Pelvic LN irradiation		83 (13.83%)
	Oropharyngeal irradiation		8 (1.33%)
	Splenic irradiation		14 (2.33%)
	Mediastinal irradiation		29 (4.83%)
	Localized chest wall irradiation		31 (5.17%)
	Palliative spinal irradiation		68 (11.33%)
	IFRT		24 (4%)
Chemotherapy and Radiotherapy			174 (29.00%)

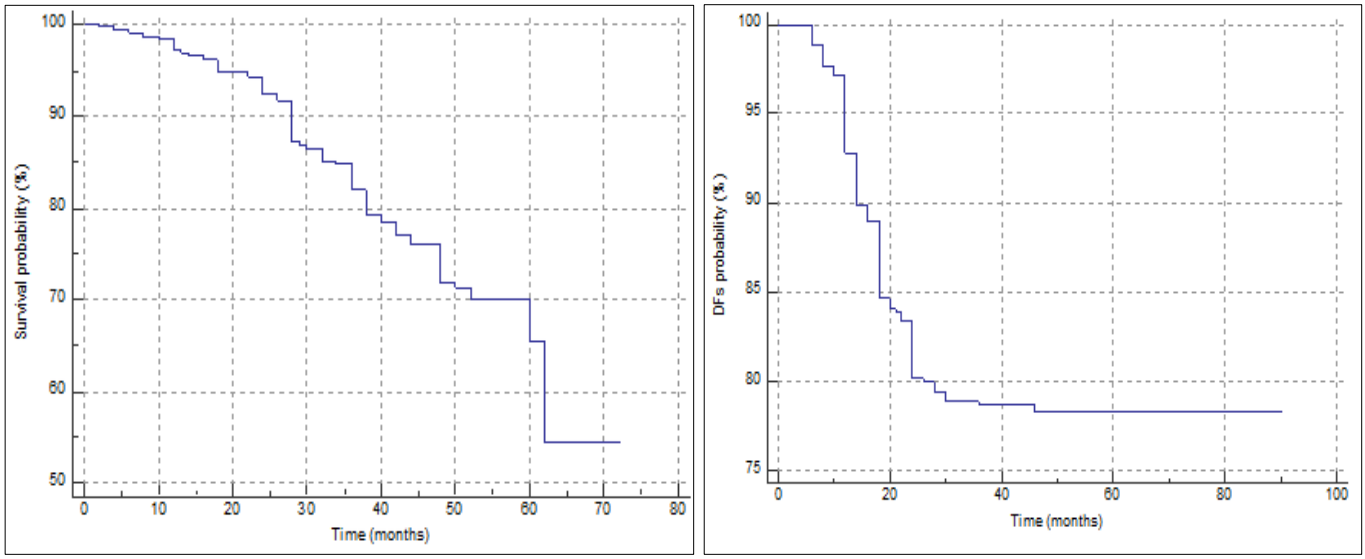
Data are presented as frequency (%). LN: lymph nodes, HL: Hodgkin Lymphoma, MM: Multiple Myeloma, NHL: Non-Hodgkin Lymphoma, IFRT: Involved Field Radiation Therapy. Lost follow up occurred in 70 (11.67%) patients. Mortality occurred in 133 (22.17%) patients. Table 4.

Table 4: Lost follow up and mortality of the studied patients

	N=600
Lost follow up	70 (11.67%)
Mortality	133 (22.17%)

Data are presented as frequency (%)

The mortality rate was in 133 (24.77%) patients with mean value (95% CI) of 58.556 (56.33 - 60.77). Regarding DFs, relapse occurred in 120 (20.00%) patients with mean value (95% CI) of 74.185 (71.665 - 76.705). Figure 2.



A B

Fig 2: Kaplan Meier for (A) overall survival analysis and (B) Disease-Free Survival of the studied patients

Discussion

The population is ageing quickly, placing a greater load on the health system and increasing the rate of malaria cases. Worldwide, the rise of malignant tumours has been attributed to changes in population and epidemic patterns [7]. According to the current study, the patient diagnosis showed that ALL was present in 6% of patients, 0.67% of patients were AML, 1% of patients were diagnosed with CML, 0.17% of patients were CLL, 13% of patients were HL, 25.33% of patients were MM and 53.83% of patients were NHL/DLBCL. In 2019, Zhang *et al.* [8] the most prevalent hematological cancer was leukemia followed by NHL then MM, and HL. The different results could be attributed to the different populations and sample sizes.

In the present study, regarding the diagnosis of the studied patients over the period (2016-2020), the diagnosis of ALL increased from 3.25% in 2016 to 11.32% in 2019 and decreased to 7.32% in 2020. The diagnosis of AML increased from 0.65% in 2016 to 0.88% in 2018 with no diagnosis of AML in 2019 and 2020. CML diagnosis increased from 1.95 at 2016 to 2.44% at 2020. The MM diagnosis increased from 24.68% at 2016 to 39.02% at 2020. The diagnosis of HL, and NHL/DLBCL decreased from 5.58% and 53.9% respectively in 2016 to 12.2% and 39.02% respectively in 2020. The WHO Lymphoma Update USA (TRUE), which includes immunophenotypic and molecular criteria for lymphoma, may enable the early discovery of previously unidentified lymphoma subtypes, which may lead to overestimation of infection rates [9]. In line with our results on chemotherapy and radiotherapy, Mandloi *et al.* [10] said that the study comprised 95 individuals with newly diagnosed DLBCL. Immunophenotypic subtype data were available for 71 patients (74.7%). According to the cell of origin, GC type was detected in 24 patients (25%), non-GC type was detected in 47 patients (50%) and unknown in 24 patients (25%). 70% of the patients received R-CHOP and 1. 1% received radiotherapy.

In the present study, the mean follow-up period was 40.5±13.24 months and the mortality rate were 24.77% with a mean value 58.556 of (95% CI 56.33 - 60.77). Also, regarding DFS, relapse occurred in 20.00% with a mean value 74.185 of (95% CI 71.665 - 76.705). Regarding HL, relapse occurred in 12.16% with a mean value of 54.421 (95% CI 50.98 -57.85).

The five-year survival rate for MM patients improved from 30% in 1990 to 60% in 2019, whereas the five-year survival rate for AML patients increased from 10% in 1990 to 35% in 2019, as per disease-specific statistics released in the Nordic nations. This is because HM therapy has advanced, including the development of new targeted drugs, immunotherapy, and better chemotherapy [11]. The death rates of other haematologic tumours, with the exception of leukaemia, appear to be steady, according to Zhang *et al.* [8]. This may be because of changes in the global population structure during the previous 30 years.

According to the current study, Regarding MM, relapse occurred in (20.57%) with mean value of 55.216 of (95% CI

52.91 -57.52). Regarding NHL/DLBCL, relapse occurred in (26.69%) with a mean value of 53.532 (95% CI 51.86 - 55.21). In a previous study by Mohan *et al.* [12] on MM cases followed up for 10 years, a total of 2055 individuals were enrolled and treated according to different treatment plans; 658 of these patients underwent follow-up care for at least ten years after their original trial enrolment. The study found that a total of 14 out of 53 patients passed away during follow-up; seven of these patients had aggressive relapses and presented with focal lesions detected on imaging; the time to death from relapse was 3.2 years (range: 0.3 - 6.0). Variations in treatment modalities and follow-up periods may have an impact on the time of relapse. Conversely, Wang *et al.* [13] discovered that participants with DLBCL alone at diagnosis had a comparable frequency of DLBCL relapse (6.3% at 5 years) compared to those with concomitant indolent lymphoma at diagnosis (5.2%; P =.46). One of the study's shortcomings was the tiny sample size.

Because of this study was retrospective one, there was an opportunity of missed data, incomplete recorders of patients, and it was a single center study.

Conclusion

An analysis of the long-term survival data in relation to the most common treatment modalities enabled a graphic evaluation of the potential variables affecting 5-year survival.

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Conflict of Interest: None.

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