

## Distribution of Hematological Neoplasia Diagnosed by Bone Marrow Morphology in Adult Patients Attending Medical City Teaching Hospital

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### ABSTRACT:

#### BACKGROUND:

The hematological malignancies are clonal diseases that derive from a single cell in the marrow or peripheral lymphoid tissue that has undergone genetic alteration; they represent approximately 7% of all malignant diseases.

#### OBJECTIVE:

Assessment for the frequency of the hematological neoplasia diagnosed by bone marrow morphology in adults patients attending Medical City-Baghdad.

#### PATIENTS AND METHODS:

This is a retrospective cross sectional study carried out in Teaching Laboratories of Medical City-Baghdad during the period from 1/1/2017 to 1/1/2018. All the cases of hematological neoplasia were diagnosed by the morphology of peripheral blood, bone marrow aspirate and /or biopsy were included in the study.

#### RESULTS:

Out of 2266 bone marrow examinations carried out in 2017 year, 570 patients (25%) were diagnosed as Hematological Neoplasia and included in the study; The frequency of HN was as follow: Acute Myeloid Leukemia:19.3% , Non-Hodgkins Lymphoma: 15.7 % , Acute Leukemia (unclassified morphologically):15.6%, Multiple Myeloma: 14%, Chronic Myeloid Leukemia:10.3%, Chronic Lymphocytic Leukemia:4.5%, Acute Lymphoblastic Leukemia: 4.4%, Myeloproliferative Neoplasia: 4.2%, Lymphoproliferative Disorders:3.3%, Primary Myelofibrosis: 2.6%, Essential Thrombocythemia: 1.9%, Hairy Cell Leukemia:1.7% ,Myelodysplastic Syndrome:1.2%, Chronic Myelomonocytic Leukemia: 0.5%, Plasma Cell Leukemia: 0.4%; 489 (86%) patients were diagnosed by bone marrow aspirates while 81(14%) patients were diagnosed by bone marrow biopsy.

#### CONCLUSION:

The most common hematological neoplasia was Acute Myeloid Leukemia followed by Non-Hodgkins Lymphoma while the least was Plasma Cell Leukemia. Patients with Acute Myeloid Leukemia, Acute Lymphoblastic Leukemia and Chronic Myeloid Leukemia presented at lower age than other hematological neoplasias. The majority of hematological malignancies were diagnosed by bone marrow aspirates.

**KEYWORDS:** Acute Myeloid Leukemia, Acute Lymphoblastic Leukemia, Chronic Lymphocytic Leukemia

### INTRODUCTION:

The hematological malignancies are clonal diseases that derive from a single cell in the marrow or peripheral lymphoid tissue that has undergone genetic alteration; they represent approximately 7% of all malignant diseases <sup>(1)</sup>.

WHO classify hematological neoplasia into myeloid and lymphoid; the myeloid neoplasia includes myeloproliferative neoplasm (MPN), Myelodysplastic syndrome(MDS), and Acute Myeloid Leukemia (AML), while lymphoid neoplasia includes precursor lymphoid

neoplasms, mature B-cell, T-cell neoplasms and Hodgkins Lymphoma (HL) <sup>(1,2)</sup>.

Factors such as genetic inheritance, environmental life style, some viral infection, drugs, radiation, and chemicals will influence the risk of developing malignancy but most cases of leukemia and lymphoma appear to result simply as a result of acquisition of critical genetic changes <sup>(1)</sup>.

The diagnosis of a hematological neoplasm usually starts from a clinical suspicion. A blood count and blood film is an essential first step whenever hematological neoplasm is suspected. The next step is depending on the specific

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condition that is suspected. A bone marrow aspirate is indicated in virtually all patients with Acute Lymphoblastic Leukemia (ALL), AML, Chronic Myeloid Leukemia (CML), MSD, and Multiple Myeloma (MM). A bone marrow trephine biopsy is indicated whenever there is a dry tap and it is necessary in Hairy Cell Leukemia (HCL), Primary Myelofibrosis (PMF), pancytopenia, leucoerythroblastic blood film, Non-Hodgkins Lymphoma (NHL) and HL.

Immunophenotyping based on flow cytometry, immunohistochemistry and immunocytochemistry is of major importance in hematological diagnosis, in addition to cytogenetic and molecular genetic analysis<sup>(3)</sup>.

### AIM OF THE STUDY:

Assessment for the frequency of the hematological neoplasia diagnosed by bone marrow morphology in adults patients attending Medical City-Baghdad.

### PATIENTS AND METHODS:

This is a retrospective cross sectional study carried out in the National center of Teaching Laboratories of Medical City-Baghdad in the period between 1-1-2017 and 1-1-2018. All the cases of hematological neoplasia diagnosed by the morphology of peripheral blood, bone marrow aspirate (BMA)-using Leishmann stain and bone marrow biopsy (BMB)-using Haematoxyline and Eosin stains were included in the study. The main studied points were the frequency of each hematological neoplasia, the ages of presentation, the distribution of gender and the comparisons between the cases which were diagnosed by BMA and/or BMB. The diagnosis of the neoplasia was carried out by a specialized hematopathologists.

### Statistical analysis:

The data was presented by frequency distribution, and means and standard deviations were made for selected variables.

The statistical significance of the association between two numerical or categorical variables was assessed by t-test and an estimate was considered statistically significant if the p value was  $\leq 0.05$ .

### RESULTS:

Out of 2266 bone marrow examinations carried out in 2017 year, 570(25%) patients were included in the study; those patients were diagnosed as Hematological Neoplasia (HN) by morphology of Peripheral Blood (PB) and Bone Marrow Aspirate (BMA) and/or biopsy (BMB); the median of age of patients included in this study was 51 years (mean 49+/-16 SD) with range of 14-89 years.

The males were 326 patients (57%) with median age of 50 years (mean 49+/- 17), while the females were 244 patients (43%) with median age of 51 years (mean 50+/-16) and males to females ratio was 1.3:1. There was no significant difference between the age of males and females.

The frequency of HN was as follow: AML: 19.3%, NHL: 15.7%, AL (unclassified morphologically): 15.6%, MM: 14%, CML: 10.3%, CLL: 4.5% , ALL: 4.4%, MPN: 4.2%, LPD: 3.3%, PMF: 2.6%, ET: 1.9% , HCL: 1.7%, MDS: 1.2% , CMML: 0.5% , PCL: 0.4% . The Myeloid Neoplasia(AML, CML, MPN, PMF, ET, MDS and CMML) diagnosed in 229 patients (40%) with median age of 46 years (mean 45+/-17 SD) and range of 19-80 years; 122(53%) patients were males with median age of 42(mean 44 +/-6.7) years, and 107 patients (47%) were females with median age of 50 years (47 +/- 5) and male to female ratio was 1.1:1. There is no significant difference between the means of age for males and females.

The most common myeloid neoplasia was acute myeloid leukemia (AML) followed by chronic myeloid leukemia (CML) while the least myeloid neoplasia was chronic myelomonocytic leukemia (CMML) –table 1.

The means ages of patients with MPN, MF, MDS and MDS/MPN (CMML) found in 6<sup>th</sup> and 7<sup>th</sup> decades of life and are significantly higher than the means ages of patients with AML and CML that were in 5<sup>th</sup> decade of life.

The lymphoid neoplasia(NHL, MM, CLL, ALL, LPD, HCL and PCL) diagnosed in 252 patients (44%) with median age of 54 years (mean 56 +/- 15) and range of 14-89 years; 152 patients (60%) were males with median age of 60 years (mean 55 +/- 2.1 SD) and 100 patients (40%) were

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females with median age of 58 years (mean 56+/-17) and male to females ratio was 1.5:1. There was no significant difference between the means of the ages for males and females. The mean of age of lymphoid neoplasia was significantly higher than that of myeloid neoplasia.

The most common lymphoid neoplasia was NHL followed by MM, while the least one was PCL- table 2.

The medians and the means of age for NHL, MM, CLL, LPD, HCL and PCL are in the 6<sup>th</sup> decade of life and were significantly higher than that of ALL which was in the 4<sup>th</sup> decade of life.

**Table 1: the distribution of myeloid hematological neoplasia**

The myeloid neoplasm	Patients No.	Median of the age in years	Mean of the age (+/- SD) In years	Range of the age in years	Ratio of males to females	% in all Hematological Neoplasia	% in Myeloid neoplasia
AML	110	40	43(17)	15-80	1.1:1	19.3	48
CML	59	41	44(11)	21-68	1.6:1	10.3	25.8
MPN	24	50	52(16)	19-61	1:1	4.2	10.5
PMF	15	65	58(17)	30-77	1:1.6	2.6	6.6
ET	11	50	51(12)	30-71	1:1.2	1.9	4.8
MDS	7	67	61(16)	30-80	2.5:1	1.2	3.0
MDS/MPN CMML	3	53	64(5)	60-80	1:2	0.5	1.3
<b>Total</b>	<b>229</b>	<b>46</b>	<b>46(17)</b>	<b>19-80</b>	<b>1.1:1</b>	<b>40 %</b>	<b>100 %</b>

AML (Acute Myeloid Leukemia), CML(Chronic Myeloid Leukemia), MPN(Myeloproliferative Neoplasia), PMF(Primary Myeloid Fibrosis), ET(Essential Thrombocythemia), MDS(Myelodysplastic Syndrome), CMML(Chronic Myelomonocytic Leukemia).

**Table 2: the distribution of lymphoid hematological neoplasia**

The lymphoid neoplasia	Patients No.	Median of the age in years	Mean of the age (+/- SD) In years	Range of the age in years	Ratio of males to females	% in all Hematological Neoplasia	% in all lymphoid neoplasia
NHL	90	51	56(16)	16-80	1.6:1	15.7	35.7
MM	80	60	60(12)	42-89	1:1	14	32
CLL	26	61	55(8)	43-74	2.7:1	4.5	10
ALL	25	30	32(16)	14-66	2.1:1	4.4	10
LPD	19	57	54(11)	25-82	1.1:1	3.3	7.5
HCL	10	57	50(8)	44-82	2.3:1	1.7	4.0
PCL	2	52	52(2)	50-53		0.4	0.8
<b>TOTAL</b>	<b>252</b>	<b>58</b>	<b>55(15)</b>	<b>14-89</b>	<b>1.5:1</b>	<b>44 %</b>	<b>100 %</b>

NHL(Non-Hodgkins Lymphoma), MM(Multiple Myeloma), CLL(Chronic Lymphocytic Leukemia), ALL(Acute Lymphoblastic Leukemia), LPD(Lymphoproliferative Disorders), HCL(Hairy Cell Leukemia), PCL(Plasma Cell Leukemia).

Eighty nine patients (15.6%) were diagnosed as acute leukemia and did not specify whether myeloid or lymphoid on morphological criteria; their median age was 25 years (mean 38+/-16). Regarding the leukemia as a special entity, 324 patients were diagnosed as leukemia; they constitute 57% of all hematological neoplasia;

226 patients were diagnosed as acute leukemia, they constitute 70% of all leukemias and 40% of all hematological neoplasia; their median of age was 37(mean 39 +/- 18) years; 131(58%) males with median age of 32 years (mean 37+/-19) and 95(42%) females with median age of 43 years (mean43+/-18) and male to female was 1.4:1.

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There is no significant difference between the ages of males and females with acute leukemia.

Regarding chronic leukemias, 98 patients were diagnosed as chronic leukemia; they constitute 30% of all leukemias and 17% of all hematological neoplasia ; their median of age was 50 years (mean 50+/-13); 63 males with median age of 50 years (mean 51+/-18) and 35 females with median age of 49 years (mean 49+/-24); there was no significant difference between the ages of males and females.

The mean of age in the chronic leukemias is significantly higher than that of acute leukemias.

The most common chronic leukemia was CML (18% of all leukemias), followed by CLL (8% of all leukemias), followed by HCL (3% of all leukemias ) and the least common was CMML (0.9% of all leukemias).

The majority of the hematological neoplasia diagnosed by bone marrow aspirate; 489 (86%) patients diagnosed by bone marrow aspirates while 81(14%) patients were diagnosed by bone marrow biopsy-table 3.

**Table 3: the frequency of diagnosis by BMA and BMB for each hematological neoplasm**

The disorder	No. & % Diagnosed by aspirate	No. & % Diagnosed by biopsy	The disorder	No. & % Diagnosed by aspirate	No. & % Diagnosed by biopsy
AML	110(100)	0	CML	57(97)	2(3)
AL	89(100)	0	MM	72(90)	8(10)
CLL	26(100)	0	LPD	14(73)	5(23)
ALL	25(100)	0	HCL	7(70)	3(30)
MDS	7(100)	0	NHL	57(64)	33(36)
CMML	3(100)	0	ET	7(63)	4(37)
PCL	2(100)	0	MPN	13(57)	11(46)
			MF	0	15(100)
			<b>489 (86)</b>	<b>81(14)</b>	

### DISCUSSION:

This study carried out in the National Center of Teaching Laboratories of Medical City where all the bone marrow aspirate and biopsies for adult patients were reviewed. Medical city is a large center in Iraq and the hospitals in most of Iraqi governorates refer the patients to this center, especially patients with hematological malignancies; so the study of hematological malignancies in those patients will give an idea about the situation in Iraq.

The study showed that hematological neoplasia(HN) constitutes 25% of the bone marrow examinations and this result give an idea about the size of these malignancies.

The study showed that the most frequent hematological neoplasia was AML which constitutes 19% of all hematological neoplasia with median age of 40 years and range of 16-80 years with slight male predominance; other studies showed nearly similar results; Al-Husseiny 2008 studied 126 Iraqi patients with AML, where their mean age was 34.2 years

and range of 13-75 years with slight male predominance <sup>(4)</sup> ; also, Salman et al in 2009 studied 115 Iraqi patients with AML their median age was 35 years<sup>(5)</sup> ; these results differ from that reported in European countries where the median age of AML patients was in the 7<sup>th</sup> decade of life; according to Bain and Matutes 2010 the median age was 65 years <sup>(6)</sup> and according to Hoffbrand et al 2016 the median age was in the 7<sup>th</sup> decade of life <sup>(3)</sup>; this difference may be explained by racial and environmental factors.

The study showed that the second most common hematological neoplasia was NHL; it constitutes 15.7 % of all hematological neoplasia and with age of 51 years and the males were more than females; this results was similar to the study of Alwan et al in 2014 which showed that the median age of the patients was 51 years and males were more than females <sup>(7)</sup> but differ from Hoffbrand et al 2016 who stated that the median age of the patients was 60 -65 years <sup>(3)</sup>.

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The present study showed that the 4th most frequent HN was MM that constitute 14% of all HN with median age of 60 years with range of 42-89 years and males to females ratio was 1:1; Laubach et al 2011 stated that MM accounts for 10-15% of all hematological malignancies<sup>(8)</sup>, similarly, Hoffbrand et al 2016 stated that MM frequency was 15%; in addition, the study of Alwan in 2014 shows, nearly, similar mean of 63 years and range of 36-83 years<sup>(9)</sup>, also, Yassin in 2013 showed mean of age of 58 years<sup>(10)</sup>.

The study showed that CML was the 5th frequent HN and constitutes 18% of all leukemia cases; it was the most common chronic leukemia with median age of 41 years and was more common in males than in females; this differs from that stated by Hoffbrand et al in 2016 where CML was diagnosed in the fifth and sixth decade of life in western countries.

The present study showed that CLL is the third frequent lymphoid neoplasia (10% of lymphoid neoplasia) and it constitutes 4.5% of HN with median age of 61 years; the study of Mohammad et al in 2011 showed median age of 64 years<sup>(11)</sup>. In addition, the present study showed that CLL was the third frequent leukemia (8% of all leukemia), but it is the most frequent form of leukemia in western countries with median age of 70 years<sup>(3)</sup>.

The present study demonstrated that ALL constitute 4.4% of HN, with mean age of 32 years and predominance of male patients; this is in agreement with the study of Al-Byaa et al 2015 who studied 64 patients with ALL and showed that the mean age of males was 30 years and the mean age of females was 35 years<sup>(12)</sup>.

The present study showed that the mean age of the patients with PMF was 58 years with range of 30-77 years, and females were more than males; Alwan in 2014 showed similar mean and range of age, but equal males and females<sup>(13)</sup>.

This study showed the median age for ET was 50 years and females more than males and these results were similar to Hoffbrand et al study in 2016 where median age was 50-55 years and similarly Antonioli et al in 2010 demonstrated that the females were more than males with median age of 52 years<sup>(14)</sup>.

Hairy cell leukemia constitutes 3% of all leukemia with median age of 57 years and predominance of males (males to females 2.3:1) those results were similar to Hoffbrand et al who reported that HCL constitutes 3% of all leukemia and males to females ratio was 4:1<sup>(3)</sup>, similarly Kveitman and Arons in 2018 reported that median age was 55 years and predominance of males<sup>(15)</sup>.

Plasma cell leukemia is a rare disorder, in the present study it is the least hematological malignancy; it constitutes 0.4% of HN and 0.8% of lymphoid neoplasia and the median age was 52 years; Albarracin and Fonseca in 2011 reported that PCL frequency was 0.2% in all leukemia<sup>(16)</sup> while Larrea et al in 2013 reported median age of 52-65 years<sup>(17)</sup>.

The study showed that the majority (86%) of the hematological malignancies were diagnosed by bone marrow aspirates; this is similar to the results of Omar et al 2014 who showed that 85% of marrow aspirates yield information of diagnostic values<sup>(18)</sup>.

### CONCLUSIONS:

- 1- The most common hematological neoplasia was AML followed by NHL while the least was PCL.
- 2- The means of the ages for the patients with MPN, MF, MDS and MDS/MPN (CMML) was in 6<sup>th</sup> and 7<sup>th</sup> decades of life and are significantly higher than the means of age for the patients with AML and CML which are in 5<sup>th</sup> decade of life.
- 3- The medians and the means of age for NHL, MM, CLL, LPD, HCL and PCL are in the 6<sup>th</sup> decade of life and are significantly higher than that of ALL which was in the 4<sup>th</sup> decade of life.
- 4- CML is more common than CLL.
- 5- The majority of hematological malignancies were diagnosed by bone marrow aspirates.

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