

ISSN 2471-5026 | Open Access

RESEARCH ARTICLE

Volume 5 - Issue 1

# Correlation Hematological Malignancies in the Hadhramout Sector Pattern and Distribution

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Received: 18 Mar, 2022 | Accepted: 09 Apr, 2022 | Published: 16 Apr, 2022

**Citation:** Daakeek AM, Bahashwan AA, Bakrman AA, Al-Zaazaai AA (2022) Correlation Hematological malignancies in the Hadhramout Sector Pattern and Distribution. J Blood Disord Med 5(1): dx.doi.org/10.16966/2471-5026.129

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#### Abstract

**Objective:** To study the pattern and distribution of hematological cancers in Hadhramout sector-Yemen and compare with the findings elsewhere in the country and worldwide.

**Methods:** Descriptive study of patients with Hematological malignancies between January 2011 and December 2015 recorded in National Oncology center- Hadhramout. Cases were sub-grouped according to their lineage into lymphoid types which include Non-Hodgkin's and Hodgkin's lymphomas, acute and chronic lymphocytic leukemia and multiple myelomas, and Myeloid types which include acute myeloblastic leukemia and chronic myeloproliferative neoplasms. Patients were classified into four age groups: <18, 18-40, 41-60 and >60 years.

**Results:** 661 cases of Hematological malignancies were registered (22.6% of all cancers registered). 58.7 % males and 41.3% females, (male to female ratio of 1.4:1). Slight female predominance was found in cases of chronic myeloproliferative neoplasms. Hematological malignancies occur at a young age, with an overall median age at diagnosis of 39 years. Non-Hodgkin's lymphoma was the most common subtype (37.8%), followed by Hodgkin's lymphoma. The majority of cases were observed among the 18-40 age groups (28%). In children and adolescents <18 years old, acute lymphoblastic leukemia and acute myeloblastic leukemia were more predominant (24%, 11.4%). Multiple myeloma commonly occurred in the 41-61 age groups (57.6%). Chronic lymphocytic leukemia mostly occurred among old patients over 60 years (66.7%). Most cases were from the Hadhramout governorate (n= 507, 76.7%) and Mukalla was the most affected city.

Conclusion: The distribution of Hematological malignancies in Hadhramout is more common in adults while decreased in the elder population.

Keywords: Hematological malignant; Myeloid neoplasms; Lymphoid neoplasms; Hadhramout

#### Introduction

The Hematological Malignancies (HM) is a group of cancers that arise from a malignant transformation of cells of the bone marrow or the lymphatic system [1]. These malignancies are induced by genetic damage or mutation in somatic cells, which can result from environmental agents such as chemicals, ionizing radiation, and viruses. They have a worldwide distribution and can occur at all ages and in both sexes. Although there are differences between the various types as regards the age and sex incidence, a changing pattern in the clinical presentation and distribution has been reported in various communities over the years [2-5]. HM comprise approximately 6.5% of all cancer incidences worldwide in 2012 [6]. Although the prevalence of these malignancies is much lower in Asia and Africa than in Western countries, the incidence of these malignancies is drastically increasing in low-income settings, while these increasing trends are not observed in Western countries [7-9]. WHO predicts that the number of blood-related cancer cases would increase by

about 48% in less developed countries by 2030 as compared to 2012 [6]. In Yemen, there is no national database on hematological cancers, except for some data found in Sana'a and Aden [10-15]. In the Hadhramout sector (which includes Hadhramout, Shabwah, and Mahra governorates), there is no published epidemiology report on HM. Therefore this study aims to determine the distribution and spectrum of various HM which are encountered in the Hadhramout sector and compare it with the findings that have been reported elsewhere in the country and worldwide.

#### Materials and Methods

This is a retrospective descriptive study, with the study population consisting of all patients with hematological malignancies (HM) diagnosed between January 2011 and December 2015 in the National Oncology Center-Hadhramout (NOC)-Yemen, which usually manages all cancer cases in the Hadhramout sector. For these cases, the data collected included details such as gender, age, place of birth and residence, date of diagnosis, and type of HM.



The patients in this study were divided into four age groups: children and adolescents: <18years old, young adults: 18-40 years, adults: 41-60 years, and elderly: over 60 years. The HM was classified as Lymphoid HM which includes Non-Hodgkin's Lymphomas (NHL), Hodgkin's Lymphomas (HL), Multiple Myelomas (MM), Acute Lymphoblastic Leukemia (ALL), and Chronic Lymphocytic Leukemia (CLL), and Myeloid HM which include chronic Myeloproliferative Neoplasms (MPN), which further subcategorized to Chronic Myelogenous Leukemia (CML), Polycythemia Vera (PV), Essential Thrombocythemia (ET), Primary Myelofibrosis (PMF) and unclassifiable MPN and Acute Myeloblastic Leukemia's (AML). In the cases where no complete data about the type of HM we used the term "nonspecific".

Data collection was performed in Excel. Statistical analysis was performed using SPSS software version 21.0. For the Chi-squared test, the results are considered significant when the p-value of significance is less than 0.05.

#### Results

In this study, 661 cases of HM were registered between January 2011 and December 2015 in the center. Overall, 2909 cases of cancers were registered in the center, indicating that HM accounts for around 22.6) %661/of 2909 of all cancers recorded. The overall median age at diagnosis for all HM combined was 39 years (Table 1).

Lymphoid neoplasms were more common representing 16.6%, and myeloid neoplasms accounted for 5.2 % of all cancers recorded. NHL was the most frequent HM (8.6% of all cancer cases), with a median age of 45 years. HL was the second most common HM (3.5%, median age 30.5 years) followed respectively by chronic MPN, ALL, AML, MM, and CLL with present and median ages shown in table 1.

All combined types of HM were more common in men than in women with a male to female ratio of 1.4:1. This slight male predominance was statistically significant (p<0.04). Slight female predominance was seen in chronic MPN. NHL was the most frequent HM in both males and females (40.5% of all male HM and 34.1% of all female HM), while the second most frequent HM, in males was HL (17%) and in female chronic MPN (19%) as shown in table 2, followed respectively by ALL, AML, MM, and finally CLL in both sexes (Table 2).

 Table 1: Distribution pattern, the median age at diagnosis of HM in NOC-Hadhramout.

Median age	% of all HM	% of all cancers	N	HM & types
39	100	22.6	661	All HM
39	73.2	16.6	484	Lymphoid
45	23	5.2	152	Myeloid
45	37.8	8.6	250	NHL
30.5	15.4	3.5	102	HL
50	15.3	3.5	101	MPN
43.5	8.8	2	58	CML
57.5	3	0.7	20	ET
57.5	2.1	0.5	14	Unclassifiable
43	1.1	0.2	7	PRV
65	0.3	0.1	2	PMF
26	7.7	1.8	51	AML
56	4.2	1%	28	MM
65	1.4	0.3	9	CLL

In all age groups, lymphoid neoplasms were more common than myeloid and NHL was the most common HM diagnosed in all age groups. ALL and AML were more predominant in the age group <18years (55.6%, 37.3%) followed by the 18-40 years age group.

HL was common in the 18-40 years age group compared with other age groups, and chronic MPN was common in most age groups except the <18years age group (Table 3). MM is common in the 41-60years age group constituting (57.1%) of all MM cases. CLL is more common in the elderly >60 years age group compared to other age groups (66.7% of all CLL cases) (Table 3).

In the group of lymphoid neoplasms, NHL was the most common disease with 51.7% of all lymphoid neoplasms, followed respectively by HL (21.1%), ALL (14.9%), MM (5.8%), and CLL (1.9%). Among the 250 NHL cases recorded during the study period, only 30 cases had available information on the histological type. The analysis of those showed that diffuse large cell lymphomas were the most common (36.7%), followed by diffuse small cell lymphoma (20%) as seen in figure 1. Analysis of HL showed that among the 102 cases, 31cases had histological information. Nodular sclerosis was the predominant subtype with 45.2%, followed by mixed cellularity (32.3%) as shown in figure 2.

For myeloid neoplasms, chronic MPN was the most frequent with 66.4% of all myeloid neoplasms, followed by AML (38.2%). Among

Table 2: Distribution of male, female, M:F ratio in NOC Hadhramout.

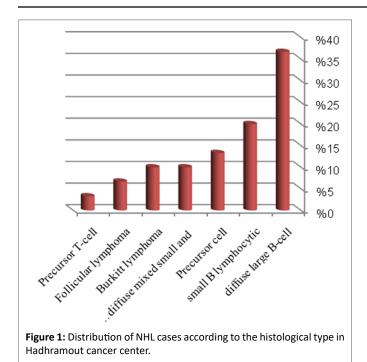
Ratio	1	emales	N	<b>Aales</b>	
M: F	N	% of female	N	% of Male	HM& Types
1.4	273	41.3	388	58.7	All HM
1.7	93	34.1	157	40.5	NHL
1.8	36	13.2	66	17	HL
0.9	52	19	49	12.6	MPN
1	29	10.6	29	7.5	CML
0.7	12	4.4	8	2.1	ET
1	7	2.6	7	1.8	Unclassifiable
2.5	2	0.7	5	1.3	PRV
0	2	0.7	0	0	PMF
1.7	27	9.9	45	11.6	ALL
1.1	24	8.8	27	4.1	AML
1.8	10	3.7	18	4.6	MM
2.1	3	1.1	6	1.5	CLL

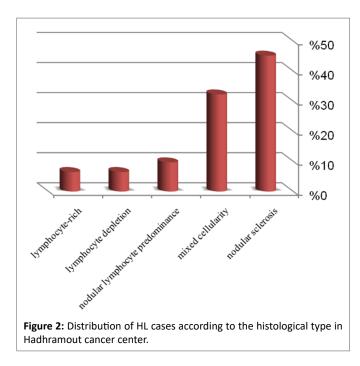
 Table 3: Distribution of HM related to age groups and sex in NOC-Hadhramout.

Type of HM	Age Groups (years)								
	<18		18-40		41-60		>60		Total
	No	%	No	%	No	%	No	%	No
NHL	51	20.4	65	26	79	31.6	55	22	250
HL	29	28.4	39	38.2	21	20.6	13	12.7	102
MPD	6	5.9	32	31.7	31	30.7	32	31. 7	101
ALL	40	55.6	18	25	4	5.6	10	13.9	72
AML	19	37.3	12	23.5	12	23.5	8	15.7	51
CLL	0	0	1	11.1	2	22.2	6	66. 7	9
мм	0	0	3	10.7	16	57.1	9	32.1	28

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subtypes of chronic MPN, the commonest was Chronic Myeloid Leukemia (CML) (46%) followed by Essential thrombocythemia (13.2%) as in figure 3. No subtype of AML could be talked about because no histological studies founded in medical records. Distributions of HM in the Hadhramout district are various. Hadhramoot governorate has the highest affected rate of all HM (n= 507, 76.7%) table 4, and the most affected area was Mukalla city (Table 5). Shabwah was the second affected governorate (n=114, 17.2%) table 3, and the most affected area was Maifaah (Table 4).

Al-Mahra was the least affected governorate (1.8%, n=12) of all HM table 4, and Saihoot was the most affected area (Table 5). NHL was the commonest HM followed respectively by HL and MPN in



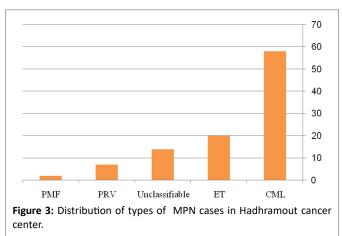


 Table 4: Distributions of HM in different governorates of the Hadhramout sector.

	Governorates						
нм	Hadhramout governorate N(%)	Shabwa governorate N(%)	Mahara governorate N(%)	Others N(%)	Total N(%)		
NHL	193 (77.2)	45(18)	4(1.6)	8(3.2)	250(100)		
HL	81 (79.4)	19(18.6)	1(1)	1(1)	102(100)		
MPN	75 (74.2)	19(18.8)	4(4)	3(3)	101		
ALL	58 (80.6)	6(8.3)	1(1.4)	7(9.7)	72(100)		
AML	39 (76.5)	7(13.7)	1(2)	4(7.8)	51(100)		
MM	22 (78.6)	4(14.3)	0	2(7.1)	28(100)		
CLL	5 (55.6)	3(33.3)	1(11.1)	0	9(100)		
Others	34 (70.8)	11(22.9)	0	(6.3)3	48(100)		
Total	507(76.7)	114(17.2)	12(1.8)	28(4.2)	661(100)		

 Table 5: Distributions of HM in common cities of Hahramout, Shabwa, and Mahra governorates.

Hadhramout gov	Shab govern		Mahara governorate		
Regions	Percent	Regions	Percent	Regions	Percent
Al-Mukalla City	22.9	Maifaah	20.2	Saihoot	33.3
Tareem	9.3	Tag	14.9	Unknown	33.3
Al-Sheher	8.5	Nasab	12.3	Al-Gaitha	25.0
Seiyun	8.5	Unknown	11.4	Geshen	8.3

Hadhramout and Shabwah governorates while NHL and MPN were the commonest in Al-Mahra (Table 4).

### Discussion

To our knowledge, this may be the first study on all HM in Hadhramout sector. It was carried out using data collected from the only center for the management of cancer patients. It presents for the first time the relative frequency of several types of HM compared to all cancers in this sector of Yemen and universal.

A total of 661 cases of HM were recorded at the NOC- Hadhramout-Mukalla- over the 5 years under review, constituting 22.6 of all cancers cases. This result is similar to those of Sana, Aden [13,16,17], Saudi Arabia [18- 20], Oman [21], India [22], and Iran [23], but higher than



what found in Morocco [24,25], Nigeria [26] and Korea [7]. We found that lymphoid neoplasms are the most common, accounting for 78.1% of all HM. This result is similar to those observed in North America, Australia, Europe, Africa, and Asia [24,27-31].

In our study, men are slightly more affected by HM than women, with a male to female ratio of 1.4:1. Such ratio is similar to those reported in Saudi Arabia (1.4:1), Morocco (1.1:1), France (1.2:1) and in the United Kingdom (1.3:1) [20,28,30]. However, the sex ratio was much higher in Bangladesh (2.2:1) and Senegal (1.6:1) [31,32]. Although there is a slight male predominance among HM overall, the sex ratio varied between age groups. In our study, a strong male predominance with a male to female ratio of 1.7:1 was observed in the age group <18 years. Several studies in developing countries have shown that HM in children often affects boys more than girls [25,33]. We found that the majority of hematological cancer cases have been observed among patients aged 18 years and over (74.7% of HM) with an overall median age at diagnosis of 39 years that resembles what occurred in Asia. For example, in Bangladesh, the median age was 42 years [32]. In Western countries, HM usually affects elderly people, for example, in the United Kingdom, the median age at diagnosis was 70.6 years [28]. NHL was the most frequent common HM (37.8%) in this study, resembles finding in cancer registries of Sana [17], and most Asian countries like Saudi Arabia [18,20,34], Jordan [35], Korea [7], and Morocco and other African countries [8,24-26], while in United States, Australia, and Bangladesh, leukemia cases were the most frequent HM [6,22,32,36] . NHL was more common in men than in women with a male to female ratio of 1.7:1 and this was similar to a previous study in lymphomas in Hadhramout [37] and other studies in Saudi Arabia but less ratio (1.2:1) was found in Oman [21,38]. We observed that the median age of NHL was 44 years which was similar to studies done in Sana, Saudi Arabia, Oman, and Jordan [17,35,39]. In our study, diffuse large cell lymphoma was the most common form of NHL (36.7%), which was consistent with other studies in Hadhramout, Saudi Arabia, Jordan, Oman, India, and Morocco [22,24,25,35-40].

HL was the second most common blood cancer in the Hadhramout sector after NHL, accounting for 15.4 % of all HM. This frequency is lower than that observed in the previous study done in Hadhramout and studies in Sana, Aden, Oman, Saudi Arabia, India, and Morocco [17-19,25,37,38,40-42], but it is higher than those observed in China, Japan, Korea, Bangladesh, Nigeria, United States and France [26,30,32,43-46].

HL occurred at all ages with a peak (38.2%) in young adults (age 18-40 years) followed by children and adolescents (age less than 18years) were present was 28.4% of all patients with HL in age groups. This age distribution resembles that of developing countries where the first peak occurs in children (under 20 years), probably because of an earlier infection with the Epstein-Barr virus in children living in those countries [32,43,47].

The most common type of HL was nodular sclerosis followed by mixed cellularity similar to the lymphoma study done locally in Hadhramout [37], and other studies in Saudi Arabia [38], China [45], and Korea [43] but differ from studies in Oman and India where mixed cellularity was the commonest type [22,40]. On the other hand, HL is much more frequent in men than women with a male to female ratio of 1.8:1, resembling other studies, with a male to female ratio ranging between 1.5 and 4.8:1 [43,45,48-50]. Chronic MPN constituted 15.3% of all HM in our study.

This frequency resembles that reported in Morocco, France, and the UK [25,28,30]. We found that chronic MPN was slightly predominant

in women, with a male to female ratio of 0.9:1. A female predominance was observed mainly in less than 18 years, with slight male predominance in patients more than 40 years. Female predominance was observed also in Morocco, the United Kingdom, and France [25,28,30]. We also found that chronic MPN was more common in adults and the elderly but only very few cases were found in younger patients. The mean age of diagnosis was 50 years, which is lower than the one observed in France [30].

The commonest chronic MPN was CML observed in 46% of all MPN and 8.8% of all HM, which was less than that seen in the Sana study [11,14] Pakistan [51], and Bangladesh [32]. Adult > 18 years was more affected with the age group 18-40 being the commonest age group affected (43.1%) like that seen in Bangladesh, with an equal M: F ratio unlike other studies [32]. ET was the second most common chronic MPN and affect older adults >60 years old. PMF was the least chronic MPN and just two female cases more than 40 years old were affected.

ALL constituted 10.9% of all HM. This frequency is consistent with those reported in some Asian countries such as Bangladesh (14.1%) [32] and one other study done in Pakistan (19.15%) [51], while lower than that found in Sana (39.1%) [11], Saudi Arabia (36.23%) [20], Oman (34%) [52], another study in Pakistan (38.1%) [4] and Ethiopia (46.3%) [5], but higher than in Aden (4%) [13], Morocco (2.4%) [25], France (2.7%) [30] and the UK (2%) [28]. ALL is generally most common in childhood and its age incidence curve is bimodal, with a peak in childhood and another peak in old age [30,49,53]. Our study showed that the first peak occurred in the patients <18 years age group (55.6%), and young adults 18-40 years age group (25%), and another peak in older age >60 years (13.9%). The sex ratio is higher (1.7:1) than in other studies done in Morocco and Nigeria (ratio 1.3:1) [30,31] and England (1.2:1) [48].

AML constituted 7.7 % of all HM. This frequency is higher to that seen in Aden (4%), Morocco (4.9%) and Nigeria (4.95) [13,25,26], but it is comparable to those reported in France (7%), UK (6.68%), United States (12%), and lower than in Sana (25.4%), Bangladesh (28.3%) and Oman (34%) [11,28,30,32,52,54]. We found that AML is more common in men than in women with a male to female ratio of 1.1:1 which is comparable to what was found in other studies [28,30,32,51,53,55]. Our study also showed that AML affected patients less than 18 years more than young adults and adults (equally 23.5%), while the elderly were less affected (15.7%), with a median age of 26 years. However, in Western countries, AML generally affects elderly people with a median age of 65-67 years [56,57]. In France, for example, 60.6% of AML was observed in people aged 60 years and over [30]. A different picture is observed in Asia, where AML affects young adults with a median age at diagnosis of 30 years in India and 35 in Bangladesh [22,32].

MM is an uncommon blood cancer in Hadhramout, accounting for 4.2% of all HM. This frequency of MM is somewhat similar to those in some Asian countries such as Saudi Arabia (5.8%) and Pakistan (5.3%) [20,58-60], and some African countries such as Nigeria [26], differ from those seen in Morocco (12.4%) [25], Bangladesh [32], and western countries such as the United States (13%), France (13.7%), and UK (10.5%) [28,30,61]. We found that men were more affected with MM than women, with a male to female ratio of 1.8:1, which was nearby to other studies [26,32,48,58,59,61]. The frequency of MM increased mainly in the adult age group (41-60 years ) at 57.1%, while only 32% in patients aged over 60 years, this differs from what is seen in other studies that MM increased with age [32,51,58]. The overall median age at diagnosis was 56 years, which is similar to Asian countries where the median age is around 55 years [32,59,62,63] but it is lower compared



to Western countries, where the median age is between 65 and 70 years [64]. In this study, CLL is a rare HM, constituting only 1.4% of all HM. This frequency is lower as compared to those observed in Sana (26.5%) [14] and Asian countries [4,32,65,66], and very lower as compared to what had been reported in Western countries [28,29,56]. The median age at diagnosis for CLL was 65 years. This result is intermediate between the results found in Western countries (median age of 70-72 years) and Asia (median age of 59-60 years) [28,30,32,66,67]. We found that the frequency of CLL increased with advancing age to 66.7% in patients aged over 60 years, which is similar to other studies. There is a male predominance among CLL, with a male to female ratio of 2.1:1, which is to studies reported from India (3:1), Bangladesh (2.9:1), Ethiopia (3.6:1), and Western countries (1.5-2:1) [30,32,56,66,68].

Most cases were from the Hadhramout governorate (76.7%) but other governorates of the Hadhramout sector had a very low percentage. This may result from treatment of many cases in other country cancer centers rather than Hadhramout (common in patients from Shabwa governorate) and outside countries especially in Gulf states (patients from Al-Mahra governorate) due to relations and a lot of immigrant people from it. The distributions of HM was the same in all governorates with MPN more in Al-Mahra and Shabwa, while the cities were the most affected areas, perhaps due to large population, availability of medical facilities, easy reach to NOC-Hadhramout, and higher medical education.

## Conclusion

This study provided for the first time the pattern and distribution of HM in Hadhramout. HM occurred at a relatively young age, with an overall median age at diagnosis of 39 years. Overall, men were more affected with HM than women, with a male to female ratio of 1.4:1. NHL was the most common HM accounting for 37.8% of all HM, followed by HL, MPN, ALL, AML, MM, and CLL in descending order. The majority of HM cases had been observed among patients aged 18-40 years (28% of all HM), followed by patients <18years and adults 41-60 years (equally 25.3%), then elderly patients over 60 years (21.4%). In children and adolescents, NHL and ALL were the most frequent HM. Hadhramout was the most affected governorate, and the large cities were the most affected areas.

# Acknowledgments

We are grateful to the clinical team and all administrative staff at the NOC-Hadhramout for allowing their health facilities to participate in the study and for their support, especially the Director of NOC-Hadhramout Dr. Zaki Sanoon for help and support to complete this study. The authors also thank Mr. Alla Awad Muftah for providing the data and correcting and reevaluation of it.

### **Ethical Consideration**

Permission and approval of the hospital committee were obtained and consent was taken from each participant. All data were dealt with confidentiality.

# Funding

No.

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