

# Leukemia Epidemiology in Karbala province of Iraq

Ahmed Mjali	
Haider Hasan Jaleel Al-	Baghdad University, College of Medicine, Baghdad, Iraq.
Shammari	
Nareen Tawfeeq Abbas	Department of Hematology, Hiwa hematology/Oncology
	Hospital, Sulaymaniyah, Iraq.
Zahraa Deheyaa Azeez	Gynecology and Obstetrics Teaching Hospital, Karbala,
	Iraq.
Saja Khudhair Abbas	Department of Hematology /Oncology, Al- Hussein Medical
	City, Karbala, Irag.

**Objective:** Investigate epidemiology of leukemia in Karbala province of Iraq, compare and identify possible changes with other populations.

**Methods:** This was retrospective descriptive study for more than 400 leukemia patients in Karbala province from November 2011 to May 2018 with evaluation of age, gender distribution, types distribution and frequency distribution types of leukemia according to age and gender.

**Result:** About 402 patients with leukemia were retrospectively enrolled in this study at median age of 30 years. Males accounted for a higher proportion of leukemia patients, 58.2 % compared to 41.8% females, with a male to female ratio of nearly 1.4:1. Acute lymphoblastic leukemia (ALL) was the most prevalent in the study group, contributing 41% (median age 10 years), followed by chronic myeloid leukemia (CML) 24.1% (median age 42 years), acute myeloid leukemia (AML) 19.2% (median age 36 years) and chronic lymphocytic leukemia(CLL) of less frequent type which contributed only 15.7% (median age 60 years).

**Conclusion:** This is the first statistical study of leukemia in Karbala. It can be used as basic information to investigate epidemiological characteristics, to evaluate progress in recent years and to develop future leukemia strategies. More statistical leukemia analyses in Iraq are needed.

### Introduction

In 2012, there were about 352,000 new cases of leukemia (2.5 percent of all new cancer cases) and 265,000 deaths (3.2 percent of all cases). The lowest incidence rates in Middle and West Africa (les s than 3 per 100,000 males and less than 2 per 100,000 females) and the highest in North America and Australia / New Zealand (more than 10 per 100,000 males and 7 per 100,000 females).Sub Sah aran Africa's estimated low incidence rates may be due to a failure to diagnose the disease in old or very young patients [1].

In Iraq, leukemia represents the fourth common cancer in both male and female. In 2009 Iraqi Cancer Board recorded 13951 cases of leukemia in Iraq in the years from 1991 to 2009 representing 6.59% of new cases [2]. In Karbala province which is a town in central Iraq, about 100 km southwest of Baghdad (Figure 1)<sup>[3]</sup>, and has an estimated population of 1013254 people in 2009 , leukemia was the sixth common cancer with incidence rate 3.26 /100000Population [2].



Figure 1. Map of Iraq3.

Leukemia is usually had four main categories, with different presentations and outcomes: acute lymphocytic leukemia, chronic lymphocytic leukemia, acute myeloid leukemia, and chronic myeloid leukemia. Males have a slightly higher incidence of leukemia than females. Leukemia rates also var y geographically and ethnically. In the US, the Caucasian incidence is higher than in African - Americans and Hispanics. The lowest rate of incidence among Americans / Alaskans [4].

Ionizing radiation exposure, chemicals like benzene, pesticides, chemotherapy, smoking cigarettes, viral infection and genetic disorders are recognized as leukemia risk factors [5][6][7][8][9][10][11]. However, these risk factors can only explain minority cases and the etiology of leukemia remains largely unknown [12].

In this study, we investigated leukemia distribution among the population in Karbala province of Iraq from 2011 to 2018. It can help to provide basic information to investigate epidemiological characteristics, to assess progress in recent years and to develop future leukemia treatment strategies.

# **Materials and Methods**

We conducted a retrospective, descriptive, epidemiological study of leukemia patients in the Karbala province, diagnosed between November 2011 and May 2018. The data for this study were obtained from the cancer registry department in Al Hussein Cancer Centre in Karbala, which was established in November 2011 and there were no accurate leukemia data available before. This Centre covers Karbala population and most of children and adults with leukemia were referred to this center for treatment. It is presently the only available source of information and most of the patients with leukemia attended the center were enrolled in this study. Data provided information about the gender of patients, diagnosis and the years of diagnoses.

Diagnoses were made on peripheral blood films and morphology of bone marrow including cytochemical staining and immunophenotyping. Patient with the non-conclusive result was excluded from this study. The selected topic was accepted by the scientific committee; official acceptance was taken from health authorities to conduct this study. Collected information was kept confidential.

#### **Statistical analysis**

The statistical package for social sciences (SPSS) for Windows, version 24 was used for entering, managing and analysis of data. Descriptive statistics presented as count (frequency), proportions, median and interquartile range (IQR), findings presented in tables and figure using MS-office software version 2013.

## **Results**

A total of 402 patients diagnosed with leukemia were retrospectively analyzed during our study. Patients ages were between 1 year and 90 years, 234 were males (58.2%) and 168 were females (41.8%), with an M/F ratio of 1.4:1. Among all leukemia cases, 22.6% (n = 91) were below 10 years. The median age of diagnosis was 30 years for all cases (Table 1).

Variable Count %
------------------



Age (year	≤ <u>1</u> 0	91
	11 - 20	72
	21 - 30	43
	31 - 40	43
	41 - 50	44
	51 - 60	42
	61 - 70	47
	> 70	20
	Median (IQR*)	30 (12 - 54)
Gender	Male	234
	Female	168

#### Table 1. Age and gender distribution of 402 cases of leukemia reported during the period 2011 - 2018.

\*IQR: Interquartile range

Regarding the distribution of types of leukemia, ALL was the more prevalent type among the studied group, contributed (41%, median age 10 years), followed by CML (24.1%, median age 42), AML (19.2 %, median age 36 years) and the less frequent type was CLL which contributed only (15.7%, median age 60 years) [Figure 2 & Table 2].

#### Figure 2. Distribution of types of leukemia of 402 cases during the period 2011 - 2018.

Leukemia types	Number of cases	Distribution(%)	Median age(year)



ALL	165	41%	10
CLL	63	15.7%	60
AML	77	19.2%	36
CML	97	24.1%	42
Total	402	100	30

Table 2. Distribution pattern, median age at diagnosis of leukemia in Karbala province.

The distribution of types of leukemia according to age group revealed that ALL was the more prevalent type of leukemia among the younger age groups it was found in 87.9% of leukemia cases in the age  $\leq$  10 years.AML was more prevalent in the age groups 31 – 40 years, and 61 – 70 years where it was found in 32.6% and 31.9% of cases in these two age groups, respectively.

CLL was more prevalent among those aged more than 50 years old with 45% of leukemia cases. Interestingly, none of the cases at the age of 30 years or below had CLL. For the CML was prevalence among those 41-50 years presenting 50% while representing only 2% of leukemia in patients below 10 years old (Table 3).

		Type of leukemia							
		ALL		AML		CLL		CML	
Age (year)		Count	%	Count	%	Count	%	Count	%
≤ 10	91	80	87.9	9	9.9	0	0.0	2	2.2
11 - 20	72	50	69.4	15	20.8	0	0.0	7	9.7
21 - 30	43	19	44.2	7	16.3	0	0.0	17	39.5
31 - 40	43	7	16.3	14	32.6	3	7.0	19	44.2
41 - 50	44	4	9.1	8	18.2	10	22.7	22	50.0
51 - 60	42	3	7.1	5	11.9	21	50.0	13	31.0
61 - 70	47	1	2.1	15	31.9	19	40.4	12	25.5
> 70	20	1	5.0	4	20.0	10	50.0	5	25.0
Gender									
Male	234	101	43.2	42	17.9	39	16.7	52	22.2
Female	168	64	38.1	35	20.8	24	14.3	45	26.8

 Table 3. Frequency distribution types of leukemia according to the type, age and gender from 2011 to 2018.

## **Discussion**

The quality and ability to access to the health systems can explain the geographical differences in leukemia, although etiological factors including gene-environment interactions would probably play a role. Global leukemia rates in males were generally higher than females with a total M/F of 1:4, which was the same as in our study [13].

In our study ALL was the more prevalent type among the studied group; contributed 41%, followed by CML 24.1%, AML 19.2%, and the less frequent type was CLL which contributed only 15.7%. In a study done in Sulaymaniyah province of Iraq, ALL was the most common type of leukemia with 44% in all cases, CML was the second type with 20% of cases followed by CLL, 18% and AML, 17% [14].

In Croatia, the most common type of leukemia was CLL, which accounted for 42% of leukemia, followed by AML with 27%, ALL with 17% and CML with 14% [15]. In Bangladesh, on the other

hand, AML was the most prevalent hematological malignancy 28.3% followed by CML 18.2 %, ALL 14.1 % and CLL 3.7 % was the least common [16].

In Karbala ALL was the more prevalent type of leukemia among the younger age groups of 30 years or below; it was found in 87.9% of leukemia cases in the age  $\leq 10$  years with a median age of 10 years. This is close to the study done by (Elew et al., 2009) in Baghdad that showed ALL represent 90.5% of leukemia cases below 10 years old [17]. This result was also closed to data in the United States with a median age of only 15 years and about 60% of patients were under 20 years of age. Although in India, about 60 to 85% of all reported leukemia was ALL [18][19].

Incidence of AML in North America, Oceania, and Europe is relatively common, whereas adults AML in Latin America and Asia is uncommon. AML affects older people with a median age at present in Western countries around 65 years [4][20]. While in our study median age was only 36 years old that closer to the previous study in Baghdad with ~33years and studies in Bangladesh with~ 35 years and India with ~30 years [16][21][22].

The median age of CML in Karbala was 42 years, which is older than the previous study done in Iraq with a median age of  $\sim$  37 years. Our result was closer to the median age in Turkey 46 years and Bangladesh was 40 years old. Interestingly much younger than of US with a median age of 65years and Europe 55 years old [16][23][24][25][26][27].

CLL is a rare hematological disorder in Asia, although it represents the most common leukemia in the West that affects elderly people. In the US, for example, CLL accounts for about  $\sim$ 34% of leukemia cases [4][28].

CLL median age in Karbala was 60 years old and none of the cases at the age of 30 years or below, this close to previous studies in Iraq with median age  $\sim$ 60 years [29]. Our result also was closer to the median age in Turkey with 63 years, India median age with  $\sim$ 60 years and Bangladesh 60 years old [16][30][31][32].

While our study median age was younger than that in the USA, Europe, and Australia which is approximately 70 years of age [32][33][34].

In conclusion the distribution of leukemia in Karbala differs from other countries, with younger median age than western countries. This may be explained by the fact that > 58% of the population under 25 years old and about 3.4% of the population above 65 years [35]. More studies are needed to understand the leukemia patterns and dissemination in Iraq and recognize biology, genetics & possible risk factor in Iraqi patients.

# Acknowledgements

We would like to thank Mrs.Afnan Al Wakeel and Mr. Hekmat Hamada Baqir from Karbala Cancer Registry Center, without their help this study couldn't see the light of day.

# References



### References

- Ferlay Jacques, Soerjomataram Isabelle, Dikshit Rajesh, Eser Sultan, Mathers Colin, Rebelo Marise, Parkin Donald Maxwell, Forman David, Bray Freddie. Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. International Journal of Cancer. 2014; 136(5)DOI
- 2. Iraqi Cancer Board. Result of Iraqi Cancer Registry 2009.Baghdad: Iraqi Cancer Registry Center, Ministry of Heaith.2012.
- 3. ThomasBrinkhoff: city population [cited 2018 June 4].Available from:http://www.citypopulation.de/Iraq-Cities.html.
- 4. Rodriguez-Abreu D, Bordoni A, Zucca E. Epidemiology of hematological malignancies. *Annals of Oncology.* 2007; 18(Supplement 1)<u>DOI</u>
- Leuraud Klervi, Richardson David B, Cardis Elisabeth, Daniels Robert D, Gillies Michael, O'Hagan Jacqueline A, Hamra Ghassan B, Haylock Richard, Laurier Dominique, Moissonnier Monika, Schubauer-Berigan Mary K, Thierry-Chef Isabelle, Kesminiene Ausrele. Ionising radiation and risk of death from leukaemia and lymphoma in radiation-monitored workers (INWORKS): an international cohort study. *The Lancet Haematology*. 2015; 2(7)DOI
- 6. Rothman N, Smith MT, Hayes RB, Traver RD, Hoener BA, Campleman S, Li GL, Dosemeci M, Linet M, Zhang L, Xi L. Benzene poisoning, a risk factor for hematological malignancy, is associated with the NQO1 609C→ T mutation and rapid fractional excretion of chlorzoxazone. *Cancer Res.* 1997; 57(14):2839-2842.
- 7. Ma Xiaomei, Buffler Patricia A, Gunier Robert B, Dahl Gary, Smith Martyn T, Reinier Kyndaron, Reynolds Peggy. Critical windows of exposure to household pesticides and risk of childhood leukemia.. *Environmental Health Perspectives*. 2002; 110(9)DOI
- 8. Ezoe Sachiko. Secondary Leukemia Associated with the Anti-Cancer Agent, Etoposide, a Topoisomerase II Inhibitor. *International Journal of Environmental Research and Public Health*. 2012; 9(7)DOI
- 9. Brownson Ross C.. Cigarette Smoking and Adult Leukemia. *Archives of Internal Medicine*. 1993; 153(4)DOI
- 10. zur Hausen H. Viruses in human cancers. Science. 1991; 254(5035)DOI
- 11. Hamblin TJ, Davis Z, Gardiner A, Oscier DG, Stevenson FK. UnmutatedIg VH genes are associated with a more aggressive form of chronic lymphocytic leukemia. *Blood*. 1999 ; 94(6):1848-1854.
- 12. Deschler Barbara, Lübbert Michael. Acute myeloid leukemia: Epidemiology and etiology. *Cancer.* 2006; 107(9)DOI
- 13. Miranda-Filho Adalberto, Piñeros Marion, Ferlay Jacques, Soerjomataram Isabelle, Monnereau Alain, Bray Freddie. Epidemiological patterns of leukaemia in 184 countries: a population-based study. *The Lancet Haematology*. 2018; 5(1)<u>DOI</u>
- 14. Karim Zhala AA, Khidhir Karzan G, Ahmed Rebaz A, Hassan Halgord A, Karim Dana Omer. Leukemia Study in Sulaymaniyah Province, Kurdistan, Iraq. *Chinese Medical Journal*. 2016; 129(2)DOI
- 15. Novak Ina, Jakšić Ozren, Kuliš Tomislav, Batinjan Katarina, Znaor Ariana. Incidence and mortality trends of leukemia and lymphoma in Croatia, 1988-2009. *Croatian Medical Journal*. 2012; 53(2)<u>DOI</u>
- 16. Hossain Mohammad Sorowar, Iqbal Mohd S, Khan Mohiuddin Ahmed, Rabbani Mohammad Golam, Khatun Hazera, Munira Sirajam, Miah M Morshed Zaman, Kabir Amin Lutful, Islam Naima, Dipta Tashmim Farhana, Rahman Farzana, Mottalib Abdul, Afrose Salma, Ara Tasneem, Biswas Akhil Ranjan, Rahman Mizanur, Abedin AKM Mustafa, Rahman Mahbubur, Yunus ABM, Niessen Louis W, Sultana Tanvira Afroze. Diagnosed hematological malignancies in Bangladesh a retrospective analysis of over 5000 cases from 10 specialized hospitals. *BMC Cancer*. 2014; 14(1)DOI
- 17. Mohammad Taghreid Kheder, Mahmood Asmaa Hashem, Elew Genan Fadel, Al-Khalidi Saja Jehad. A STUDY ON THE PREVALENCE OF ACUTE LEUKEMIA AMONG A GROUP OF IRAQI PATIENTS. Journal of Al-Nahrain University Science. 2009; 12(2)DOI



- 18. National Cancer Institute, Cancer Stat Facts (2015). Acute Lymphoblastic Leukemia[cited 2018 June 5]. Available from: https://seer.cancer.gov/statfacts/html/alyl.html.
- 19. Arora RS, Eden TOB, Kapoor G. Epidemiology of childhood cancer in India. *Indian Journal of Cancer.* 2009; 46(4)<u>DOI</u>
- 20. Linet MS, Devesa SS, Morgan GJ. The leukemias. In Cancer epidemiologyand prevention.3rd edition. *Edited by Schottenfeld D, Fraumeni J Jr. NewYork: Oxford University Press.* 2006;841-871.
- 21. Bhutani Manisha, Vora Amish, Kumar Lalit, Kochupillai Vinod. Lympho-hemopoietic Malignancies in India. *Medical Oncology*. 2002; 19(3)<u>DOI</u>
- 22. Muhsin SY, Al-Mudallal SS. Expression of Aberrant Antigens CD7 and CD19 in Adult Acute Myeloid Leukaemia by Flow Cytometry. *Iraqi J Hematology*. 2014; 3(1):1.
- 23. Alameri A, Khudhair M, Batool G, Murad N. Epidemiology of chronic myeloid leukemia in Iraqi patients. 14th Congress of the European Hematology Association Abstract Book haematologica. 2009; 94(s2):P 578.
- 24. Sahin Fahri, Saydam Guray, Comert Melda, Uz Burak, Yavuz Akif Selim. Turkish Chronic Myeloid Leukemia Study: Retrospective Sectional Analysis of CML Patients. *The Turkish Journal of Hematology.* 2013; 30(4)DOI
- 25. National Cancer Institute, Cancer Stat Facts (2015).Chronic myeloid leukemia [cited 2018 June 30].Available from:https://seer.cancer.gov/statfacts/html/cmyl.html.
- 26. Tardieu Sophie, Brun-Strang Catherine, Berthaud Patrice, Michallet Mauricette, Guilhot François, Rousselot Patrice, Sambuc Roland. Management of chronic myeloid leukemia in France: a multicentered cross-sectional study on 538 patients. *Pharmacoepidemiology and Drug Safety.* 2005; 14(8)DOI
- 27. Alwan AF. Assessment of cytogenetic response after treatment with imatinibmesylate in patients with chronic phase chronic myeloid leukemia. *Iraqi J Hematology.* 2014; 3(1):56-61.
- 28. American Cancer Society: Cancer facts & amp; figures 2012. Atlanta: American cancer society. [Cited 2018 July 13]. Available from:http://www.cancer.org/research/cancerfactsfigures/cancerfacts-figures-2012.
- 29. Naji AS. Outcome of 49 Iraqi adult patients with Chronic Lymphocytic Leukemia treated with oral alkylating agent. *J Fac Med Baghdad*. 2012; 54(2):126-130.
- 30. Pamuk Ömer Nuri, Pamuk Gülsüm Emel, Soysal Teoman, Öngören Şeniz, Başlar Zafer, Ferhanoğlu Burhan, Aydin Yldz, Ülkü Birsen, Aktuğlu Gulten, Akman Nuran. Chronic Lymphocytic Leukemia in Turkey: Experience of a Single Center in Istanbul. *Southern Medical Journal*. 2004; 97(3)DOI
- 31. Saxena R, Kumar R, Sazawal S, Mahapatra M. CLL in India May Have a Different Biology from That in the West. *Blood*. 2016; 128(22):5574.
- 32. Gogia Ajay, Sharma Atul, Raina Vinod, Kumar Lalit, Vishnubhatla Sreenivas, Gupta Ritu, Kumar Rajive. Assessment of 285 cases of chronic lymphocytic leukemia seen at single large tertiary center in Northern India. *Leukemia & Lymphoma*. 2012; 53(10)<u>DOI</u>
- 33. National Cancer Institute, Cancer Stat Facts (2015).Chronic lymphocytic leukemia[cited 2018 July 30]. Available from: https://seer.cancer.gov/statfacts/html/clyl.html.
- 34. World health organization, Union for International Cancer Control (2014) .Chronic lymphocyticleukemia[cited2018 August 2].Available from:http://www.who.int/selection medxicines/committees/expert/20/applications/CLL.pdf.
- Central Intelligence Agency, WorldFact Book (2017).Age Structure [cited 2018 august 6]. Available from: https://www.cia.gov/library/publications/the-world-factbook/geos/iz.html.