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Epidemiology and Patterns of Leukemia in Northern Saudi Arabia

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ABSTRACT

Objective: *The aim of the present study was to determine the patterns of leukemia in Northern Saudi Arabia.* ***Methodology:*** *This was a retrospective descriptive study conducted in King Khalid hospital, Hail, Kingdom of Saudi Arabia (KSA) including records of leukemia from 2008 to 2016.* ***Results:*** *The overall Crude Incidence Rate (CIR) of leukemia was 7.45 per 100.000 person-year, including patients diagnosed with different patterns of leukemia in Northern Saudi Arabia. The mean age of patients was 45.4 years with a minimum of 5 years and a maximum of 107 years old. Around 43 (59%) were males and 30 (41%) were females.* ***Conclusion:*** *The incidence rates of leukemia are relatively higher in Northern Saudi Arabia, with an increase of all subtype.*

Keywords: Leukemia, Saudi Arabia, Acute lymphoblastic leukemia, Acute myeloid leukemia, CD19, CD10, CD22

INTRODUCTION

Leukemia is hemopoietic cancer that encompasses various biological distinctive subcategories. Leukemia has diverse geographical differences with inconsistent disease presentation and outcomes. Inconsistency might be linked to the local health system and possible etiological factors comprising gene environmental interfaces [1]. Leukemia is classified into many subtypes including acute myeloid leukemia (AML), chronic myeloid leukemia (CML), acute lymphoid leukemia (ALL), chronic lymphoid leukemia (CLL), lymphoblastic leukemia and many other precursors associated leukemia subtypes [2-4].

Many risk factors have been implicated to the etiology of leukemia. Exposure to radiation has been linked to an increased risk of ALL, AML and CML [5,6]. Genetic alterations such as in neurofibromatosis and Down syndrome were found to be associated with lymphoblastic leukemia and AML in children [5].

Environmental and occupational exposure to chemicals such as benzene and its associated products has been associated with an increased risk of adults' AML [7,8]. Maternal, as well as, the initial years of life has been associated with an elevated risk for the development of ALL [8]. Obesity parental drug use, parental alcohol use and a history of hematological cancers are also risk factors for developing leukemia [9-11].

In recent years there has been an increase in the incidence rates of leukemia, particularly among central area (Riyadh), Eastern region, and Northern region (in which this study exists) [12]. The analysis of cancer epidemiology in Saudi Arabia has significant differences in different regions [13,14], which might be attributed to the variations in the co-existence of etiological factors. As a result, the analysis of cancer incidence in Saudi Arabia validated significant differences according to gender, age, and regions of the KSA. Thus, the aim of the present study was to determine the patterns of leukemia in Northern Saudi Arabia.

PATIENTS AND METHODS

This was a retrospective descriptive study conducted in King Khalid hospital, Hail, Kingdom of Saudi Arabia (KSA) during the period from October 2016 to March 2017. Full coverage of data regarding leukemia was retrieved from the hospital, including records of leukemia from 2008 to 2016. The obtained data were filled in standard form prior to the filling on SPSS sheet for analysis. The most important parameters filled in the form were age, sex, diagnosis, and tumor markers expression.

Ethical Consent

The study was approved by the ethical committee at the College of Medicine, University of Hail. This in addition to an agreement letter was taken from King Khalid hospital authority.

Statistical Analysis

Data were analyzed using SPSS software version 16. The p-value<0.05 was considered statistically significant.

RESULTS

All over patterns of leukemia by age, sex, and clinic-pathological characteristics, during the period from 2008 to 2016, included 73 (Crude Incidence Rate (CIR)=7.45 per 100.000 person-year) patients diagnosed with different patterns of leukemia in Northern Saudi Arabia. The mean age of patients was 45.4 years with a minimum of 5 years and a maximum of 107 years old. Around 43 (59%) were males and 30 (41%) were females.

Overall, AML accounted for 12.3% of the cases (n=9; IR=1.0); CML, 19.2% (n=14; IR=1.6); ALL, 23.3% (n=17; IR=1.9); CLL, 11% (n=8; IR=0.89); leukemia unspecified 31.5% (n=23; IR=2.6); myeloid non-specified, 1.3% (n=1; IR=11); lymphoblastic non-specified, 1.3% (n=1; IR=11).

IR of AML was 14% higher among males vs females 10%; IR of CML was 26.7% higher among females vs 14% among males; IR of ALL, was similar for both sex 23.3%; leukemia unspecified males vs females was 60.9% vs 30% with a male predominance noted in most groups (Table 1 and Figure 1).

Table 1 Types of leukemia by sex

Types of Leukemia	Males	Females	Total
AML	6	3	9
CML	6	8	14
ALL	10	7	17
CLL	5	3	8
Leukemia un-specified	14	9	23
Myeloid non-specified	1	0	1
Lymphoblastic non-specified	1	0	1
Total	43	30	73

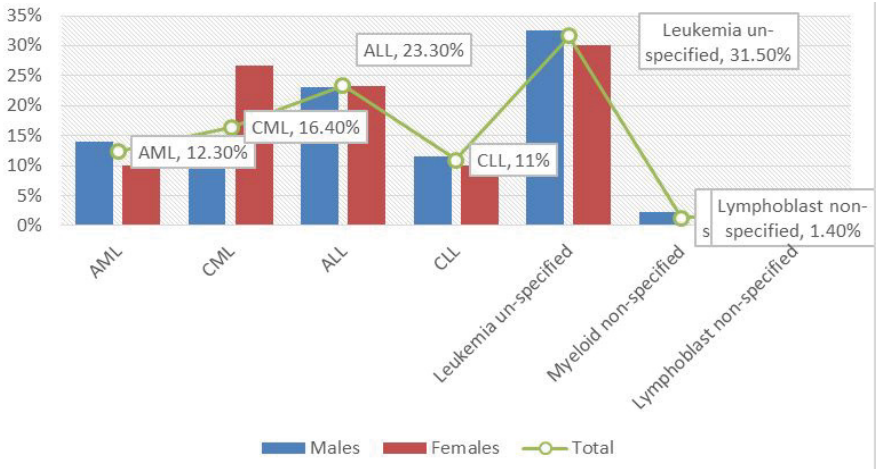

Figure 1 Proportions of the types of leukemia by sex

Higher age-specific IR of AML was 77.8% (31-40 years); CML, 35.7% (41-60 years); ALL, 58.8% (<18 years); leukemia un-specified, 26% (<18 years) (Table 2 and Figure 2).

Table 2 Types of leukemia by age

Types of Leukemia	<18 years	19-30 years	31-40 years	41-60 years	61-75 years	76+ years	Total
AML	1	1	6	1	0	0	9
CML	0	2	2	5	3	2	14
ALL	10	1	2	2	2	0	17
CLL	0	1	0	0	3	4	8
Leukemia un-specified	6	5	3	5	2	2	23
Myeloid non-specified	0	1	0	0	0	0	1
Lymphoblastic non-specified	0	0	0	0	1	0	1
Total	17	11	13	13	11	8	73

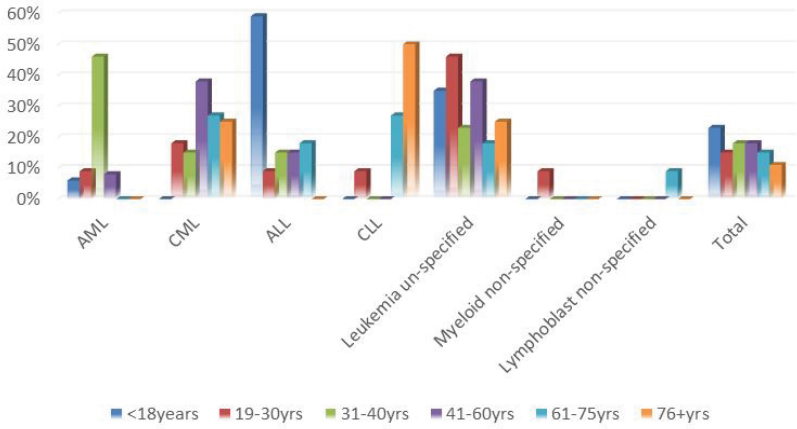

Figure 2 Proportions of the types of leukemia by age

The highest IR of leukemia was in years 2010 and 2016, the IR was 16.4%, trailed by years 2011, 2009, 2014 and 2015 revealing 15%, 12.3%, 11%, and 9.6%, in that order as shown in Figure 3.

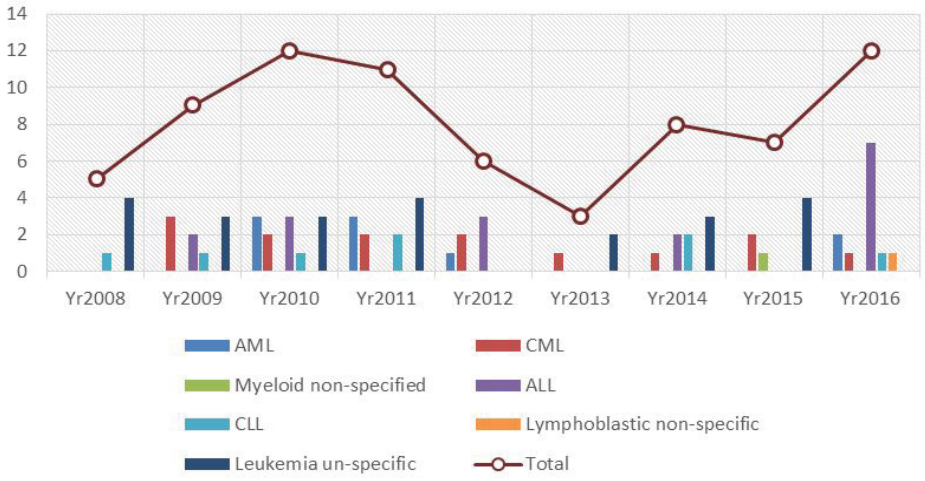

Figure 3 Types of leukemia by incidence rates by years

The tumor markers expression in different types of leukemia is summarized in Table 3. Tumour markers testing was available for 30 samples. Higher expression rates were seen with CD19, 13.3% (n=4; found among AML, CML, ALL and CLL, one positive expression in each type). CD10 expression was realised in 10% (n=3; AML, ALL, leukaemia

unspecified, one positive in each). CD22 expression was realised in 10% (n=3; AML, ALL, leukaemia unspecified, one positive in each). Other markers have exposed positive expression of <6.7%, as referred to in Table 3.

Table 3 Leukemia types by tumor markers

Marker	AML	CML	ALL	CLL	Leukemia unspecified	Myeloid non-specific	Lymphoblastic non-specific	Total
CD5	0	0	0	2	0	0	0	2
CD10	1	0	1	0	1	0	0	3
CD15	0	1	0	0	1	0	0	2
CD19	1	1	1	1	0	0	0	4
CD20	0	0	0	2	0	0	0	2
CD22	1	0	1	0	1	0	0	3
CD25	0	0	0	2	0	0	0	2
CD33	0	0	0	0	1	0	0	1
CD34	1	0	0	0	0	0	0	1
CD35	0	0	1	0	0	0	0	1
CD45	0	0	1	0	1	0	0	2
CD56	1	0	0	0	0	0	0	1
CD58	1	0	0	0	0	0	0	1
CD66	1	0	0	0	0	0	0	1
CD117	0	0	0	0	1	0	0	1

Normal discharge was executed for the majority of patients 56% (n=41; including leukemia unspecified 29.3%, CML and ALL 19.5%, CLL 17%, AML 9.8%) (Table 4). Discharge against medical advice (DAMA) was indorsed for 28.8% (n=21; including leukemia unspecified 42.9%, CML 23.8%, ALL 19%, AML 9.5%) (Table 4). About 11% of the patients were transferred to other oncology centers and approximately 4% of the patients died, as indicated in Table 4.

Table 4 Outcomes by leukemia types

Leukemia types	DAMA	Normal discharge	Transferred	Died	Total
AML	2	4	2	1	9
CML	5	8	0	1	14
ALL	4	8	4	1	17
CLL	1	7	0	0	8
Leukemia unspecified	9	12	2	0	23
Myeloid non-specific	0	1	0	0	1
Lymphoblastic non-specific	0	1	0	0	1
Total	21	41	8	3	73

DISCUSSION

Knowledge of patterns of leukemia in a burdensome geographical area may predict etiologic hypotheses for disease control and effectual management. The overall incidence rate of leukemia in this series is relatively higher from other reports from Saudi Arabia. A study described the incidence of leukemia from 2001 to 2008, reported the highest incidence rate from Riyadh (5.2 per 100.000 for males) followed by Eastern and Northern (study area) regions at 4.5 per 100.000 males. The highest overall incidence rate among females (4.5 per 100.000) was found in Najran (Southern region) [12]. Reference to these former statistics, the present findings (7.45 per 100.000) sign posts an incessant boost in the epidemiology of leukemia in Saudi Arabia in over-all and Northern in particular.

The leading leukemia subtype in Northern Saudi Arabia was ALL (23.3% with IR=1.9). Although there is a lack of data regarding leukemia subtypes from Saudi Arabia individual studies have buoyed up a predominance of ALL over the other subtypes [15-17]. Likewise, it was reported that ALL is most common leukemia subtype among children under 15 years worldwide [18,19]. Many factors may have a direct or indirect link to the etiology of ALL in Saudi Arabia. Obesity, which is a risk for ALL is melodramatically growing in Saudi Arabia, particularly among the younger population because of the cumulative custom of unhealthy fast food, as suggested by a study from Saudi Arabia [20,21]. With the scarcity of studies pertaining to the etiology of ALL from Saudi Arabia, the genetic and

clinical features, as well as, treatment outcome is analogous to what is seen in western countries [22,23]. In this study, ALL was more common among males compared to females. Similar results were previously reported [15]. Likewise, the bulk of the cases were ascertained amongst the younger population, which was in line with published data [15].

The present study ranked the CML (19.2%) as a second leukemia subtype after ALL. The global incidence of CML is ranging from 7% to 20% of all leukemia cases with a median age of presentation at 45-55 years [24,25]. Limited literature was reported from Saudi Arabia in this regard [26]. CML was predominantly realized at age range 41-60 years. Though CML can be perceived in all age groups studies have publicized greater incidence rates among relatively elder population [27,28].

AML (12.3% (n=14; IR=1.0)) ranked as a third leukemia subtype after ALL and CML in this series. It was well recognized that AML is the commonest leukemia in adults [29]. Infections during childhood through adulthood, in addition to several genetic and environmental factors, have been linked to the etiology of AML [30,31]. Reports from Saudi Arabia have suggested similar risk valuation and clinical outcomes of AML equated to those in the western world [32,33]. Although AML can occur in all age groups, in the present study it was more frequently seen in patients at age range 31-40 years [34].

A number of cases of non-specified leukemia (31.5%) were reported in the present study. These cases may conceal phenomenal genetic mutations, which might further be ascribed to diverse etiology.

To foretell the genetic orientation and subsequent disease management, leukemia's markers were done for a group of patients. The greatest expression was noticed with CD19. Most of leukemias and lymphomas with B-lineage possess CD19 as a surface antigen [35]. Chimeric antigen receptor modified T-cells against CD19 have potent anti-leukemic activity [36]. CD10 and CD22 ranked the second expressed markers in this study. It was found that most of ALL cases positively express CD10 marker [37]. Anti-CD10 monoclonal antibodies can be used to cure acute leukemia [38]. On the other hand, CD22 (a B-lineage antigen) is considered a principal therapeutic target for ALL [39].

The outcome of patients seemed to be scrupulous with the view of the findings in this study designating felicitous overall management of the disease. Although the present study has exploited important information for future management of leukemia in northern Saudi Arabia but has some limitations, including its retrospective setting.

CONCLUSION

The incidence rates of leukemia are relatively higher in Northern Saudi Arabia, with increasing of ALL subtype. Presence of ample integer of unspecified leukemia obliges the necessity for more investigations to recognize whether there are rare previously unreported genotypes.

DECLARATIONS

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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