



Pattern and Age Distribution of Leukemia in Sudan- Retrospective Analysis

Amar A Dowd^{1*}, Salah OM²

¹Department of Hematology, University of Medical Science and Technology, Sudan

²Sudan Radioisotope Center, Sudan

Abstract

Low income countries in sub-Saharan Africa are experiencing a rapidly growing cancer burden, and leukemia account for 6.9% of death rate from cancer in the region. So far there are no comprehensive descriptions reporting of diagnosed leukemia in Sudan. This is a hospital based retrospective descriptive study (RICK) from 2009 till 2013. The main aim of this study is to reflect the burden of hematological cancer and the epidemiological data based on the demographic characteristic (age, sex, and frequency of hematological cancer). Morphological typing was done according to FAB classification. Result reveal total of 2535 registered patients aged between 1 to 97 years had been diagnosed with malignant hematological disorder (Leukemia). A 58.1% were male (n=1474) and 41.9% (n=1061) were female with male to female ratio of 1.3 to 1.0. The overall mean age at diagnosis was 40 years. Chronic myeloid leukemia was the most frequent (32.3%) with the mean age of 44.5 years followed by AML 42.8% mean age of 35.1 years, ALL represent 21.1% with the mean age 19.3 while CLL 21.7% with mean age 60.8. This study presents the pattern and distribution of leukemia. It shows the differences in the population as compared to other settings with lower prevalence of CLL and ALL, women might be under reported. Further genetic and epidemiological study is highly recommended.

Keywords: Leukemia; French American British; Acute lymphoblastic leukemia; Acute myeloid leukemia; Chronic myeloid leukemia

Abbreviations

FAB: French American British; ALL: Acute Lymphoblastic Leukemia; AML: Acute Myeloid Leukemia; CML: Chronic Myeloid Leukemia

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*Correspondence:

Amar A Dowd, Department of Hematology, University of Medical Science and Technology, Khartoum, Sudan, Tel: +249-910800639; E-mail: ammared@gmail.com

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Introduction

The common cause of disability and death in low income countries (sub-Saharan Africa) is cancer [1]. Many factors contributing to increasing the burden among them is aging, social and behavioral trends, HIV, and other endemic infections [2]. An estimated 43,050 new cases of leukemia diagnosed in 2010, with approximately 21,840 related deaths [3]. One of the ten most frequently occurring cancers Leukemia, including Acute and Chronic Myeloid Leukemia (AML and CML), Acute and Chronic Lymphocytic Leukemia (ALL and CLL) [4,5]. Incidence rate of reported Leukemia cases were generally 20% to 25% higher among male than females [6]. The projected cases would bear global burden of more than 21.7% million new cancer cases and 13 million cancer deaths by 2030 [7]. The status of cancer in Sudan is largely unknown as there is recently established population-based cancer registry but still challenges related to the diagnosis and reporting of cases may play a role in the pattern observed [8]. According to global data hematological malignancy is the second most common cancer in Sudan, 2012 [8]. Leukemia is the primary cancer originating from cells of the bone marrow and there are two main categories including, acute leukemia of myeloid or lymphoid origin and chronic leukemia of myeloid or lymphoid origin. The causes of leukemia malignancy remain obscure but it's believed to be linked to certain environmental exposure such as chemicals, pesticides, benzene, smoking, ionizing radiation and infectious diseases [9]. The incidence of leukemia various among different geographical, and demographic characteristic [10]. In case of Sudan, there is no published report so far addressing the incidence of leukemia. Understanding the epidemiology of hematological malignancy would surely contribute to identify the risk factors in the environment and would provide basis for devising the cancer care management and preventive strategies for this malignancy [11]. The main aim of this study is to present an overall pattern and age distribution of leukemia in Sudan.

Materials and Methods

Sudan has two-run specialized cancer hospital, in none of them there is specialized hemato-oncologist, however the majority of hematological malignancy managed in Radio-Isotope Center in KHARTOUM (RICK), there is two private hospitals available for management of hematological malignancy. While more than 70% of the population in Sudan treated in Khartoum, most of tertiary health care facilities centered in Khartoum, Leukemia is treated mostly in the RICK hospital under general oncology unit, few of cases seeking private clinics, of them only two specialized for treatment of hematological malignancy. This is retrospective hospital based analysis; the study population consists of all patients with hematological malignancies diagnosed in RICK center from 2009-2013. Data is extracted from hospital record with definitive diagnosis of leukemia. The source of information for diagnosis include clinical features, complete blood count, bone marrow morphology including cytochemical staining, immunohistochemistry and immunophenotyping in selected cases. All leukemia diagnosis was based on morphological typing carried out according to French American British Classification (FAB). Although WHO classification (2008) based mostly on immunophenotyping and molecular study, none of the centers in the country have the diagnostic facility, the study stick to FAB classification. As there is no proper and effective hospital record keeping system in Sudan, there is possibility the same patient recorded twice, these will eventually undermine leukemia cases. To eliminate these possibilities, raw data were painstakingly analyzed to clean up such duplicated and re-enrolled cases. The final data representing individual cases were analyzed by SPSS version statistical software. The protocol was ethically approved by SAUMASRI.

Results

A total of 2535 diagnosed leukemia cases extracted from RICK hospital were retrospectively analyzed in this study. Of these, patients aged between 1 and 97 years (Table 1). Regarding gender male represent 58.1% of cases while Females 41.9% (Table 2) with male to female ratio 1.3:1. Among all leukemia cases 6.7% (n=338) were children aged under 20 years old. The combined median age for all leukemia is 40.3 years (Table 1). CML is the most frequent type of leukemia 32.1% with the mean age at diagnosis of 44.5 years, followed by AML 24.8% with the mean age of 35.1 year. The least frequent cases among ALL 21.1% with the mean age 19.3 and CLL 21.7% with mean age 60.8 years (Table 3a). Moreover, sex-specific analysis was also performed for the overall and leukemia specific cases. The frequency of the type of leukemia among both sex, is dominated by CML among male 28.6% followed by CLL 24.6, then AML 23.9% while the least common is ALL 22.9%. In contrast to female CML represent 37.4% of all leukemia cases followed by AML 26.1% then ALL 18.9% while the least frequent leukemia is CLL 17.6% (Table 3b).

Discussion

To our knowledge this is the first comprehensive report on the burden of leukemia in Sudan, however data from cancer registry recently published 2015 reveal leukemia is the second most common cancer in Sudan [12]. No significant difference was observed in the median age of presentation Male 42 years; Female 41 years for both sexes. This is a hospital-based study represents the overall current country picture on leukemia. Additional population-based studies are warranted to reveal the true incidence of other HM. Unlike western countries, the leukemia seem to afflict younger population as

Table 1: Shows mean age distribution among leukemia case.

	Number	Minimum	Maximum	Mean	Std. Deviation
Age	2535	1	97	40.37	23.134

Table 2: Shows gender distribution among leukemia cases.

	Frequency	Percent
Male	1474	58.1
Female	1061	41.9
Total	2535	100

Table 3a: Shows subtypes of leukemia cases.

	Frequency	Percent
ALL	537	21.2
AML	629	24.8
CML	819	32.3
CLL	550	21.7
Total	2535	100

Table 3b: Shows mean age in each sub type of leukemia.

	Number	Minimum	Maximum	Mean	Std. Deviation
ALL	537	1	95	19.3	19.348
AML	629	1	95	35.16	22.551
CML	819	1	95	44.53	17.062
CLL	550	3	97	60.71	13.546

Table 4: Shows frequency of each subtype of leukemia according to gender.

	Male		Female	
	Frequency	Percent	Frequency	Percent
ALL	337	22.9	200	18.9
AML	352	23.9	277	26.1
CML	422	28.6	397	37.4
CLL	363	24.6	187	17.6
Total	1474	100	1061	100

is indicated by the overall median age at diagnosis was 42 years. There is clear under-representation of children in this study. It is generally argued that young age phenomenon of cancers might be due to the lower life expectancy especially in developing countries and younger population structure of a respective country [13-15]. In Europe AML presents mainly an adult's disease with a median age at presentation of 64 years, accounting for around 30% of all leukemia in adults, and ~18000 new patients are diagnosed in each year, representing ~0.6% of all cancers [16]. The annual incidence rate in Europe ranges from two per 100000/year to four per 100000/year [16]. In the past decade, the trend in overall incidence of AML has generally been stable or slowly increasing in most European countries, while most cases of CML occur in adults with a median age at presentation around age 60. CML comprises only around 2% to 3% of all the leukemia diagnosed in patients <20 years of age but the incidence increases with age slowly until the mid- 40s, then more rapidly from about one per 100000/year in children <10 years to two per 100000 in people in the fifth decade to one per 10000 at age 80. The disease is more common in males [17]. An interesting study in United Arab Emirate (UAE) found that the rate of AML among UAE female nationals was higher than in nationals' male and expatriates [18]. The study proposed

that chemicals in henna dye, which is used to decorate the body, as well as a lack of sunlight, could be behind the increased incidence [18]. Henna is applied in many African countries especially Sudan where it is used by vast majority of Sudanese married [18]. In Sudan, 42.1% of the population is under 15 years old and the median age of the entire population is 19.9 years [19]. Another reason is related to the underreporting cases of older individuals possibly because of several socioeconomic and cultural reasons. However, the lower life expectancy explanation is doubtful as in economically developing countries with much higher life expectancies similar to those seen in Western countries-are also affected by CML, at relatively young ages [18-20]. The reasons behind this phenomenon are unclear (Table 4).

However, it is likely that the multiple factors including genetic, infections and other environmental factors might play crucial role in this young age phenomenon in Sudan. Our retrospective analysis included 6.7% childhood (under 20 years) leukemia cases (n=338), of which approximately 76% cases adolescent (15 to 19 years age group) leukemia patients. It is important to mention that childhood cases were under represented in the present study as the information was obtained from the hematology department of the centers which usually did not manage childhood. Leukemia's were found to be the most common blood associated cancers, constituting of all children HM cases [20]. ALL is the most frequent cancer accounting for 37.3% (n=126) followed by AML (34%, n=115) and CML (13%, n=44). Like Western countries and India the leukemia's were the most prevalent childhood cancers with a relative proportion ranging from 25% to 40% of all childhood cancers. Studies all over the world have revealed that Leukemia is gender-skewed, often affecting men more than women [21]. This study also found that men were more involved than women, with an overall male to female ratio of 1.3:1.0. The incidence of AML in adult is relatively common in North America, Europe, and Oceania, while adult AML is rare in Sudan, Asia and Latin America [22]. AML generally affects older individuals with a median age at presentation of around 65 years in Western countries and it accounts for 29% of all leukemia's in adults in US. This study showed that acute leukemia's tend to affect relatively young adults aged 20 to 49 years 66.4% cases. The median age at onset for AML 35 years in Sudan is relatively higher than in India 30 years. Apart from lower life expectancy prevailing in the Indian subcontinent, it is likely that elderly patients may not be reporting to the hospitals because of relatively rapid progression of AML. ALL occurs in people of all ages but it exhibits bimodal age-specific curve with peaks in youngest less than 20 years and oldest ages more than 50 years. In this study more than 55% of observed ALL occurs in young adults (20 to 40 years) with a median of 27 years. In US, the overall median age for ALL is only 14 years, since approximately 60% of the cases occur in children under 20 years old. In case of adult, the median age was 38 years. Chronic leukemia's constituted 21.9% of all HM and 34% of leukemia's in Sudan. CML is the second most common type (18.2%, n=912), while CLL is the least frequent (3.7%, n=183) HM. The frequency of CML is five times higher than CLL. The pattern of CML occurrence is different in India and Africa where it is the most common form of leukemia [11]. In Sudan, the incidence of CML is very high, being the predominant cancer in men in last 25 years. CLL is a rare type of leukemia in Sudan while this is the commonest form of leukemia affecting elderly in Western countries with a median age of 70 years [10]. In US, for instance, CLL constitutes about ~34% of all leukemia [13]. In Sudan, CLL is found to occur mainly in adults (median age ~60 years). The lower frequency of CLL in Sudan and

its neighboring countries may not be associated with lower life expectancy since the incidence of CLL in Japan is at least 4 to 5 times lower than Western countries; despite Japanese have the highest life expectancy in the world. It is possible that genetics and environment may play important role in its development [10].

Conclusion

This study presents the pattern and distribution of leukemia in Sudan. It shows the differences in the population as compared to other settings with lower prevalence of CLL and ALL, women might be under reported. Further genetic and epidemiological study is highly recommended. There is no proper follow-up system to track terminally-ill patients in Sudanese hospitals. Detailed clinical data were also not available because of incomplete record keeping system. Like other low-income countries, many of these limitations are intrinsic to Sudan health system. Time-trend analysis was not also possible due to lack of homogeneity of data obtained from RICK, which has been described in the method section and elsewhere.

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