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ORIGINAL ARTICLE

A Ten Year Descriptive Study of Adult Leukaemia at Al-Jomhori Teaching Hospital in Sana'a, Yemen

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Abstract:

Background: There is scarcity of data of the epidemiology of leukaemia in Arab countries including Yemen. Understanding patterns of leukaemia underpins epidemiology and can provide insight into disease etiology. The aim of this research is to determine the epidemiologic pattern of adult leukaemia in Yemen.

Methods: The research is a descriptive cross-sectional study. We analyzed the data of 702 adult patients with leukaemia, who were newly diagnosed over a ten-year period between October 1999 and October 2009 at the referral haematology centre in Sana'a at Al-Jomhori Teaching Hospital, according to type of leukaemia, age, sex, geographic distribution and time of diagnosis.

Results: Acute Myeloid Leukaemia (AML) was found to be the most common (45.1%) followed by Chronic Myeloid Leukaemia (CML) (26.5%), Acute Lymphoid Leukaemia (ALL) (17.7%) and Chronic Lymphoid Leukaemia (CLL) (10.7%), respectively. There was an almost equal prevalence of AML and CML for males and females but males had significantly more cases of ALL and CLL ($p = 0.008$). A significant variation in geographic pattern showed that the highest number of cases is seen the Central mountainous region and the least number of cases in the South-eastern region which is coastal and lowland ($p<0.001$). The seasonal variation showed that higher number of ALL cases was seen in the summer months (33%) compared with other seasons (21% in the spring, 24.2% in autumn and 21.8% in winter).

Conclusions: The pattern of adult leukaemia in Yemen is different from that seen in western countries which could be attributed to different environmental exposure. The geographic pattern indicates a possible role of certain environmental factors which warrant further investigations. The pattern of seasonal variation needs further studies for evaluating the seasonality.

Key words: Leukaemia, Yemen, Epidemiology, Seasonality, Geography, Environmental factors

1. Introduction

Cancer has been ranked the second after cardiovascular disease as leading cause of death from chronic diseases in developing countries. In 2007, deaths due to cancer in the developing world represented five of 7.5 million of the global cancer deaths. The World Health Organization (WHO) delivered a resolution calling for improved measures of cancer prevention, early detection and treatment in all WHO member countries (1). The Republic of Yemen lacks a national cancer register and there are no reliable data available (2). However, according to the first descriptive analysis report of the data on cancer cases in Yemen registered at the National Oncology Center during 2007, leukaemia was ranked as the third most common type of cancer after breast and Non-Hodgkin Lymphoma (Unpublished data).

The etiology of leukaemia remains unknown but it may be the result of a complex interaction between host susceptibility factors and different environmental susceptibility agents (3). The incidence of particular subgroups of leukaemia varies with age and sex which may suggest differences in etiology. The most common types of leukaemia in adults are AML, CML and CLL. In contrast, chronic leukaemia is extremely rare in childhood and ALL is the most common type of childhood leukaemia. Similarly all types of leukaemia show male predominance (4, 5).

Prior cancer chemotherapy and exposure to radiation and benzene are identified as risk factors for adult leukaemia, primarily AML (6). However these risk factors for adult leukaemia account for only a small proportion of all adult cases. Results of cytogenetic studies suggest that exposure to certain environmental agents may be associated with clonal chromosomal aberrations which may play a role in the activation of cellular oncogenes (7). Environmental risk factors that have been explored and have produced inconsistent association with leukaemia include farming, proximity to nuclear plants, hair dye, exposure to pesticides and petrol products, infections and alcohol consumption (6, 7). Life style factors including smoking, obesity and some dietary factors as risk for adult leukaemia have been assessed in several epidemiologic studies (8-13). Studies on the geographical distribution of leukaemia show higher number of patients of leukaemia who lived in rural areas which suggests that risk factors do exist in the rural environment (14-16).

Elucidation of environmental and life style risk factors requires understanding patterns of leukaemia which underpins epidemiology and can provide insight into disease etiology (17). Although Asian pattern including Japan, Singapore and Hong Kong were compared with American and European pattern, there is scarcity of data of the pattern of leukaemia in Arab countries including Yemen (17, 18). It sounds interesting to know the pattern of leukaemia in these developing countries which have different life style and different environmental exposure compared to that seen in the West or Far east countries (18). Yemen occupies the southern end of the Arabian Peninsula and has low standards of living similar to the situation in many developing countries. Malaria, schistosomiasis and intestinal parasites are common and visceral leishmaniasis is present in certain regions (19). Inadequate nutrition is also prevalent and Khat cultivation and regular khat chewing is very popular in the Yemeni community. In contrast, the situation is different in the West and other developed Asian countries where high standards of living are ensured and such parasitic infections are rare. The haematology unit at Al-Jomhori Teaching Hospital in the capital city Sana'a deals with haematological diseases including leukaemia and to which cases are

referred from all over Yemen (16, 19, 20). Thus, the aim of this research was to describe the epidemiologic pattern of adult leukaemia referred to this hospital over 10 years (October 2nd 1999-October 1st 2009).

2. Methods

Subjects

This descriptive cross sectional study included adult patients 14 years of age or older diagnosed for the first time as leukaemia between October 2nd 1999 and October 1st 2009 at the Haematology Unit at Al-Jomhori Teaching Hospital in Sana'a. Exclusions were patients who were previously diagnosed or have received treatment before presentation to the unit. The study was approved by Al-Jomhori Teaching Hospital authority.

Laboratory Investigations

The diagnosis of leukaemia was identified according to the standard practice and based on at least peripheral blood and bone marrow morphology and cytochemistry (19). Immunophenotyping, cytogenetic and molecular biology studies were done when needed for confirmation of the diagnosis (19). The patients were classified as AML, ALL, CML or CLL cases.

Data analysis

Data was analysed using SPSS version 10. The association between dependent and independent variables were tested using Pearson Chi-Square test. The significance level was considered at $p < 0.05$. The time of initial diagnosis of each case was recorded to assess for seasonal variation in the occurrence of leukaemia which is more objective than the time of initial symptoms which is subjective and cannot be determined accurately. However regarding acute leukaemia the presentation is usually within a short interval and moreover we categorized the time period according to seasons and not month-wise to accommodate for the possible delay of presentation. Regarding chronic leukaemia the symptoms are usually observed over a long period of time and season related variation in diagnosis is not expected and they are considered in analysis to serve as controls for acute leukaemia. Cases were distributed according to different geographical areas in Yemen (according to the governorates including patients resident in the towns and the districts officially following that governorate). The governorates were grouped into three regions (Figure 1). The Central mountainous region of the country includes the governorates of Sana'a, Dhamar, Almahweet, Marib, Ibb, Raymah, Al-Baydha and Ad-Dali. The Southern region includes the governorates of Taiz, Hadramawt, Al-Mahrah, Lahj, Abyan, Shabwa and Aden. The Northern region includes the governorates of Al-Hudaydah, Amran, Sa'adah, Hajjah and Al-Jouf. The population of Yemen according to the last Yemen's population census data of December 2004 was 19,721,643 (21). We used this census data, which is located at the midpoint of the study period, to assess the significance of variability of geographical distribution of leukaemia in Yemen. The population of the different regions (calculated by adding the total population of all governorates belonging to each region) was 8,317,650 for the Central region, 5,744,285 for the Southern region and 5,659,708 for the Northern region (21).

3. Results

Between October 2nd 1999 and October 1st 2009, 702 patients were included in this analysis. Of the total 702 patients, AML was the most common 45.1% (317/702), followed by CML 26.5% (186/702) and ALL 17.7% (124/702). CLL was least common 10.7% (75/702). The sex distribution of leukaemia shows a male/female ratio for all types 1.2:1, almost similar numbers of males and females for both AML and CML. For ALL and CLL, the diseases were more common

among males (table 1). The results are statistically significant (χ^2 = 11.858, p = 0.008).

Table 1. Prevalence and distribution of leukaemia in Yemen over 10 years according to gender

Sex	Types of Leukaemia n (%)*				Total
	AML	CML	ALL	CLL	
Male	159 (50.2)	95 (51)	80 (64)	49 (65)	383 (54.6)
Female	158 (49.8)	91 (49)	44 (36)	26 (35)	319 (45.4)
M/F ratio	1.0	1.0	1.8	1.9	1.2
Total	317 (45.1)	186 (26.5)	124 (17.7)	75 (10.7)	702 (100)

*Chi-Square test: χ^2 = 11.858, p = 0.008

Table 2 shows the age distribution of leukaemia. AML was most common in the 40-59 years age group, similar to CML. However for ALL, the disease is most common in the 14-19 years age group and CLL is most common in the elderly (≥ 60 years). The results were statistically significant (χ2 = 486.618, p<0.001).

Table 2. Prevalence and distribution Leukaemia over 10 years according to age

Age	Types of Leukaemia n (%)				Total
	AML	CML	ALL	CLL	
14-19	52 (16.4)	8 (4.3)	62 (50)	2 (2.7)	124 (17.7)
20-29	65 (20.5)	21 (11.3)	37 (29.8)	0 (0.0)	123 (17.5)
30-39	40 (12.6)	54 (29)	9 (7.3)	1 (1.3)	104 (14.8)
40-59	96 (30.3)	70 (37.7)	13 (10.5)	23 (30.7)	202 (28.8)
≥60	64 (20.2)	33 (17.8)	3 (2.4)	49 (65.3)	149 (21.2)
Total	317 (45.1)	186 (26.5)	124 (17.7)	75 (10.7)	702 (100)

*Chi-Square test: χ^2 = 486.618, p < 0.001

The median age [range] in years was 40 [14-90] for AML, 18.5 [14-75] for ALL, 40 [16-85] for CML, 60 [18-90] for CLL and 40 [14-90] for all types.

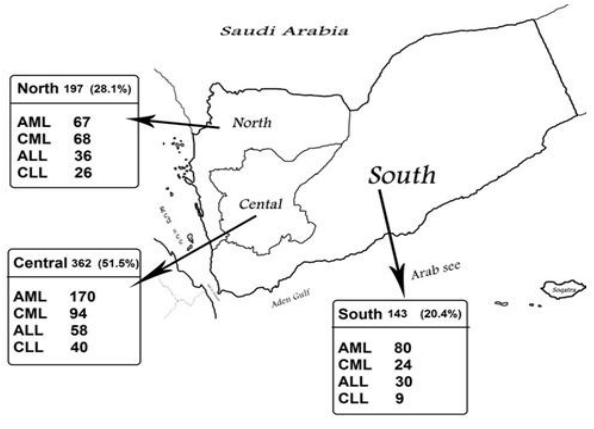
Table 3 shows the distribution of leukaemia cases according to the different seasons, spring (from 21 March to 20 June), summer (from 21 June to 20 September), autumn (from 21 September to 20 December) and winter (from 21 December to 20 March). No significant seasonal variation was noted when all leukaemia types were evaluated together (χ^2= 6.487, p = 0.69). When acute leukaemia types were evaluated separately, higher number of ALL cases was seen in the summer months (33%) compared with other seasons (21% in the spring, 24.2% in autumn and 21.8% in winter).

Table 3. Seasonal distribution of leukaemia cases in Yemen over 10 years

Season	Types of Leukaemia n (%)				Total
	AML	CML	ALL	CLL	
Spring	85 (26.8)	46 (24.7)	26 (21)	21 (28)	178 (25.3)
Summer	78 (24.6)	49 (26.4)	41 (33)	17 (22.7)	185 (26.3)
Autumn	69 (21.8)	37 (19.9)	30 (24.2)	17 (22.7)	153 (21.8)
Winter	85 (26.8)	54 (29)	27 (21.8)	20 (26.6)	186 (26.5)
Total	317 (45.1)	186 (26.5)	124 (17.7)	75 (10.7)	702 (100)

*Chi-Square test: χ^2 = 6.487, p = 0.69

Figure 1 is a schematic representation of a map of Yemen showing the geographical distribution of leukaemia cases. The Central mountainous region of the country had the highest number of leukaemia cases (362 patients) i.e. 51.5 % followed by Northern region (197 patients) i.e. 28.1 % .The least number of cases were seen in the Southern region (143 patients) i.e. 20.4 %. The Chi squared test showed a significant geographic distribution of leukaemia cases (χ^2 = 33.035, p<0.001).



Chi-Square test: χ2 = 33.035, p < 0.001

Figure 1. A schematic representation of a map of Yemen showing the geographical distribution of leukaemia cases in Yemen over 10 years (October 1999 to October 2009)

4. Discussion

This research is performed to study the epidemiology of leukaemia in Yemen. A total number of 702 cases of leukaemia were evaluated over the ten-year period (October 2nd 1999 to October 1st 2009). AML was most common followed by CML and ALL respectively and CLL was the least common constituting only 10.7% of the total number of leukaemia cases. This pattern is similar to that seen in Southeast Asia showing higher incidence of the myeloid leukaemia (AML and CML) and CLL is the least common (4, 5, 22). However, it is different from that seen in USA and other Western countries where CLL is the most common form of leukaemia (5, 22). This may indicate a different exposure to certain etiologic factors.

In this study there is a male predominance when all types of leukaemia were considered together with M/F ratio of 1.2. The male predominance is striking for ALL and CLL with M/F ratio of 1.81 and 1.88, respectively. However, there is an almost equal sex occurrence for AML and CML. The finding seen in the Western world is male predominance for all types combined and separately. The M/F in U.S. is 2 for CLL, 1.28 for ALL, 1.55 for AML, 1.73 for CML and 1.68 for all types (23). This may indicate a different environmental exposure for females in our community. Such suggestion has been raised by a study performed in United Arab Emirate where AML was significantly more common among national females (IRR: 1.93) (24). It was suggested that cumulative risk factors to which females could be exposed such as vitamin D deficiency as a result of sunlight deprivation and direct exposure to benzene and color enhancement in Henna (a herbal cosmetic used by Arab females to stain their nails, hands, feet a, legs and arms) may play a role in female predominance of adult AML incidence (24). Females in our community do share these two risk factors with other women in the Arabian Peninsula.

The age distribution of leukaemia is similar to the pattern seen in Western countries showing that AML cases increase with age, CML is a disease of the middle age, ALL is most frequent in the young and CLL is most common in the elderly group of patients. However for ALL, the second peak after 60 years of age was not seen in our study (4, 23). The median age for AML and CML in our study is 40 years compared to 64 and 60 years respectively in USA, 60 years in our CLL patients compared to 70 years in USA and it is 40 years for all types combined in our patients compared to 67 years in USA which means that our patients are in general 10 to 20 years younger which may indicate different age period during exposure to risk factors or that certain factors may delay the onset of leukaemia in Western patients (4, 22). A study on adult AML in UAE shows that the median age was 39 years which is similar to our patients indicating similar risk profile (24).

To the best of our knowledge, this is the first report in Yemen and even in the Arabian Peninsula and other Arab countries studying the geographic distribution of leukaemia. A distinct geographic pattern in the distribution of leukaemia was seen. Highest proportions of Leukaemia cases were observed in the Central region and the least number of cases were seen in the Southern region. This variation could be attributed to the habits of chewing Khat in the Northern and Central regions of Yemen considering that pesticides are used heavily for cultivation of khat to hasten its growth and consequently khat chewers are cumulatively exposed to pesticides which have been shown to be associated with leukaemia (25, 26). The adverse effects of chewing khat which is grown with

pesticides on human health were investigated in people of the mountainous areas of Yemen (27).

This study showed an increased number ALL cases in the summer compared to other seasons. This goes with other studies performed in western countries which provide evidence for seasonality and possible infectious etiology for ALL only (28-30). Further studies examining seasonality in developing countries including Yemen are recommended.

A limitation of this study is that it is a hospital based which may be affected by a referral bias which is influenced by variations in disease awareness, cultural barriers especially linked to the age and sex of the patient, inconvenience of travel and distance involved. However the fact that the study included cases during a ten year period may reduce the effect of referral bias (31). Such data are of importance providing an overview of the pattern of leukaemia in Yemen considering the fact that cancer registry has not been implemented yet in Yemen.

5. Conclusion

In conclusion, the epidemiology of leukaemia in Yemen looks distinctive concerning the finding of equal sex incidence of AML and CML. A geographical variation of distribution was documented with more Leukaemia cases in the Central region and the least number of cases is seen in the Southern region. Higher cases of ALL were recorded in the summer. The current study warrant further studies to identify the environmental and life style risk factors of leukaemia in Yemeni population to help development and implementation of protective strategies.

Conflict of interest

The authors have no conflict of interest to disclose.

Author's Contribution

JA designed the study; JA, WA, MA, AAM, and LA contributed to data collection and Laboratory analysis; JA and WA contributed to data analysis and the interpretation of results. JA drafted the manuscript. All authors read and approved the final manuscript.

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