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Pattern of Chronic Leukaemia at Shaikh Zayed Hospital, Lahore

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SUMMARY

One hundred and eleven patients of chronic leukaemia were diagnosed over of a period of 6½ years (January 1994 to June 2000), at Haematology Department of Shaikh Zayed Hospital, Lahore. Chronic leukaemias constituted 34% of the total 326 patients with all types of leukaemias diagnosed during the same period. Median age at the time of diagnosis for chronic leukaemias was 40 years (range 2 months to 80 years). Male to female ratio was 1.6:1. Chronic myeloid leukaemia (CML) accounted for 88 patients (79.3%), and chronic lymphocytic leukaemia for 23 patients (20.7%). Median age at presentation was 35 years (range 2 months to 75 years) for CML and 60 years (range 30-80 years) for CLL. One 44 years old male diagnosed as hairy cell leukaemia (HCL), was included in CLL patients. Age distribution showed a contrasting pattern for CML and CLL. CML was especially frequent in young and middle-age adults and showed a peak in 4th decade of life. CLL on the other hand, mainly occurred in people over 50 years, with a peak in 6th decade of life. Both the types of chronic leukaemias were more common in males. CLL however showed more pronounced male predominance.

INTRODUCTION

Chronic myeloid leukaemia (CML) and chronic lymphocytic leukaemia (CLL) are historically related disorders. The chronic leukaemias were first described by Bennett and Virchow in 1847[1]. Thereafter in 1851 Virchow classified leukaemia into "splenic" and "lymphatic" forms[2], which roughly correspond to CML and CLL respectively[1]. Current notions of CML and CLL were described in 1909[1].

CML is a clonal myeloproliferative expansion of transformed, primitive haematopoietic progenitor cells. It involves myeloid, monocytic, erythroid, megakaryocytic, B-lymphoid and occasionally T-lymphoid lineage[3]. The disease passes through three district phases – chronic phase, accelerated phase and blast crisis – during which the leukaemic clone progressively loses its ability to differentiate[4]. CML was the first human disease in which pathogenetic process was linked to a specific karyotypic abnormality, the Philadelphia (Ph) chromosome[3], first discovered in 1960[5-7]. CML is reported to account for about 15% of all cases of leukaemias[3,8,9], slightly more common in male, specially prevalent in young and middle aged adults[9]. A small peak in under 5 age group is observed due to juvenile CML[10,12]

CLL is a neoplastic disease characterized by accumulation of small mature appearing lymphocytes in the blood, narrow and lymphoid tissues. Generally the lymphocytes are of B-cell lineage, and in less than 2% cases of T-cell origin[11]. It is the most common adult leukaemia in Western societies, where it accounts for nearly 30% of all leukaemias[1,11,12]. In contrast CLL is rare in Asia representing less than 5% of all, the leukaemia cases[1]. It is predominantly a disease of the late middle and old age[13,14]. Rare cases have been reported in children[1].

Of all the leukaemais, the male to female ratio is highest for CLL and lowest for CML[10]. In the present study we have analyzed 111 consecutive cases of chronic leukaemia, diagnosed in the Haematology department of Shaikh Zayed Hospital,

Lahore. The frequency, age and sex related distribution pattern was evaluated and the findings were compared with other national and international studies.

PATIENTS AND METHODS

This study was conducted by the Department of Haematology, Shaikh Zayed Hospital, Lahore. During the period of this study, which extended from January 1, 1994 to June 30, 2000 (6½ years) a total of 111 new patients of chronic leukaemias were diagnosed among 326 consecutive cases of all leukaemias. All the patients were diagnosed for the first time and were included irrespective of their age, sex, social or ethnic background. Already treated or patients diagnosed elsewhere were not included. Thorough evaluation of peripheral blood and bone marrow was done to make precise diagnosis. Giemsa stained pre-treatment blood and bone marrow aspirate smears were examined in all cases.

Bone marrow trephine biopsy was also performed in selected cases. Neutrophil alkaline phosphatase (NAP) score was performed on the fresh, direct peripheral blood smears in case of CML. Tartarate resistant acid phosphatase was performed on BM and peripheral blood smear to confirm Hairy cell leukaemia (HCL). HCL was included in CLL cases. All the confirmed cases of CML and CLL were evaluated to observe their relative frequency and pattern of age and sex related distribution.

RESULTS

Amongst 326 consecutive cases of all leukaemias, chronic leukaemia accounted for 111 patients (34%) with a median age of 40 years (range 2 months to 80 years) at presentation (Tables 1, 2). CML was more frequent than CLL accounting for 88 (79.3%) and 23 (20.7%) of the 111 chronic leukaemia patients, respectively. CML / CLL ratio was 3.8:1 (Table 2). Among the major types of all leukaemias, CML was the third most frequent type accounting for 27%, after AML (32.9%), ALL (31.6%), followed by CLL (7%) and acute bilineal leukaemia (1.5%) (Table 1).

Table 1: Haematology Department, SZH, Lahore (January 1, 1994 to June 30, 2000)

Types	*Number*	*Percent*
Total cases of leukaemia	326	100
Acute leukaemia	215	66
AML	107	32.9
ALL	103	31.6
Bi-Lineal	5	1.5
Chronic leukaemia	111	34
CML	88	27
CLL	23	7

Table 2: Chronic leukaemia (n=111)

	Number	*Percent*
CML	88	79.3
CLL	23	20.7
CML : CLL	3.8 : 1	

Median age at presentation for CML was 35 years (range 2 months to 75 years) as compared to 60 years (range 30-80 years) for CLL. Overall male / female ratio was 1.6:1, whereas for CML and CLL it was 1.4:1 and 2.8:1, respectively. Table 3 depicts the complete breakdown of presenting age and sex characteristics.

Overall age related distribution of chronic leukaemia showed an early small peak in patients upto 10 years of age (first decade), than an increased frequency after 20 years, reaching a peak in 31-40 years (4th decade), followed by a sharp decline, and another peak in 51-60 years (6^{th} decade). A fall was observed thereafter in older age groups. The early small peak in first decade and the largest peak in 4^{th} decade was entirely contributed by CML, whereas 3rd peak in 6th decade was predominantly contributed by CLL patients (Table 4; Fig. 1).

Only 1 (4.3%) of CLL patients was under 40 years, whereas 66 (75%) of CML patients were upto 40 years of age. Twenty (87%) of CLL patients were over 50 years of age. CML / CLL ratio which was grossly in favour of CML in early age groups

Table 3: Presenting age and sex distribution

Type	*Sex*	*No.*	*M/F*	*Age (Years)*	
				Range	*Median*
CML	-	88	1.4	2 m-75y	35
	M	51	-	2 m - 65 y	36
	F	37	-	8 - 75	35
CLL	-	23	2.8	30-80	60
	M	17	-	30-80	60
	F	6	-	45-65	57.5
CLL+CML	-	111	1.6	2 m - 80 y	40
	M	68	-	2 m - 80 y	40
	F	43	-	8 - 75	35

was reversed in favour of CLL after 50 years. The relative frequency of CLL continued to increase progressively in older age groups (Table 4).

Table 4: Age distribution

Age (Years)	*No.*	*Age (Years)*		*CML/CLL*
		CML	*CLL*	
Upto 10	6	6	0	6:0
11 - 20	3	3	0	3:0
21 - 30	24	23	1	23:1
31 - 40	34	34	0	34:0
41 - 50	13	11	2	5.5:1
51 - 60	20	8	12	1:1.5
61 - 70	7	2	5	1:2.5
71 - 80	4	1	3	1:3
Total	**111**	**88**	**23**	**3.8:1**

One 44 years old male diagnosed as hairy cell leukaemias (HCL) was included in CLL. HCL therefore accounted for 4.3% of CLL, 0.9% for chronic and 0.3% of all leukaemia cases.

CML accounted for 7 patients (5.8%), among a total of 121 cases of all the leukaemias in children (upto 15 years of age). Only 10% of our CML patients were upto 20 years of age (Table 4).

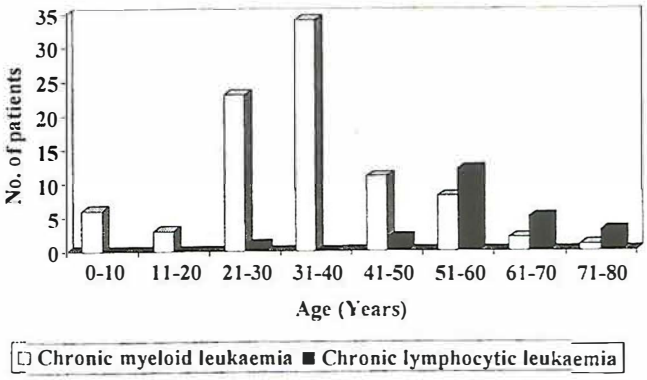

Fig. 1:

DISCUSSION

Geographic distribution

CLL

Considering the geographic distribution of chronic leukaemias, it becomes evident that CLL, which is the commonest type of leukaemia seen in the western countries [1,11,12], is quite infrequent in Asian[10], Far eastern[10,12], African[10,12] and South American[10,12] populations.

Table 5: Comparison

Authors	*Country*	*CML*	*CLL*	*No.*
Hansen et al. (1983)	Denmark	20%	40%	13,813
Kwiatkowski et al. (1994)	Poland	15%	25%	38,200
Khan et al. (1989)	S. Arabia	19%	19%	293
Al-Bahar et al. (1994)	Kuwait	15%	9%	723
D'Costa et al. (1989)	India	38%	3%	242
Ahn Yo et al. (1991)	Korea	20%	1.5%	Pop.Based
Yang (1991)	China	15%	1.09%	1670
Hassan et al. (1994)	Pakistan	26%	9.4%	234
Present study	Pakistan	27%	7%	326

*Percentage are out of all leukaemias.

The present study is in conformity with the same pattern. The frequency of CLL, which was observed to be 7% of all the leukaemias in our patients, is significantly lower than western societies and relatively higher when compared with India and other Afro Asian countries. CLL is reported to be around 30% of all leukaemia in United States[10]. Two large studies from Denmark[15] and Poland[16] report frequency of CLL to be around 40% and 25% of all leukaemias, respectively. In studies from Middle East, CLL is reported to constitute 19% and 9% of all leukaemias in Saudi Arabia[17] and Kuwait[18] respectively. From Pakistan a major study by Hassan et al. [19] reported a figure of 9.4% for CLL. CLL is reported to be even more rare in India (2.9-4.2%)[10,20] . Korea (1.5%)[21], and China (1.09%)[22]. A frequency of around 2% or less is also reported from Japan and African countries[10]. Lower frequency rates for CLL are also reported from Spain, Brazil, Columbia, Puerto Rico, Hungary, Israel and some of the Eastern European countries[10]. CLL is primarily a disease of late middle and old age. However the relative infrequency of CLL in developing countries cannot be entirely explained on low life expectancy.

In Japan where the age distribution and life expectancy is similar to the Western populations, extremely low CLL frequency suggests that this geographic pattern of CLL may in fact be dependent on combination of factors relating to, race, socioeconomic background, ethnic diversity and average life expectancy[12].

CML

In contrast to CLL, geographic distribution pattern for CML is reported to show no significant differences and rates are fairly uniform for both sexes and races[10]. In the present study CML accounted for 79.3% of the chronic leukaemias and 27% of the all leukaemia cases. This frequency when compared with other studies confirm that difference is not as marked as is observed in case of CLL. When compared with other international studies and available statistical data, it is observed that higher CML frequency rate is reported from India (38.4[20] and 56.1%[10]), whereas a lower rate is reported from Denmark (20%)[15], Saudi Arabia (19) [17], and 15% from USA[9], Kuwait[18], China[22] and Japan[10]. From another Pakistani study rate of 26.0% is almost similar to our finding. The frequency of CML and CLL reported in different studies are shown in Table 5.

Age related distribution

CLL typically occurs in people over 50 years with a median age of 60 years at presentation[1]. Our patients with CLL also presented with a median age of 60 years. On the other hand median age of presentation for CML patients was 35 years, which is lower than 44-55 years reported for western population[3,6].

Distribution of CML and CLL in different age groups demonstrated a contrasting pattern, which confirms that CLL is primarily a disease of old age

with peak in 6th decade in comparison to CML which primarily affects young and middle aged adults, with peak in 4th decade. A small peak observed in the first decade is comparable with a similar peak reported in white children, under 5 years of age[10]. Half of our patients under 10 years were upto 5 years of age. CML/CLL ratio, which was grossly in favour of CML in patients upto 50 years was reversed in patients over 50 year. Relative frequency of CLL increased progressively after 50 years of age.

A progressive decline in CML frequency after 40 years observed in our patients is in contrast to more rapid increase in middle age as reported for west[23]. Furthermore CML is reported to be a disease of middle life reaching a peak between 50-60 years in the west[12]. It therefore appears that CML affects relatively younger population in our setup. In Africa even younger population is affected with over 25% of the CML patients reported[10] to be under 20 years as compared to about 10% observed in our patients.

CLL, although less frequent than west shows a fairly similar distribution pattern in different age groups.

Sex related pattern

Male to female ratio is reported highest for CLL (1.7-2.0:1) and lowest for CML (1.0-1.1:1)[10]. A similar observation is made in our study, however male predominance is more pronounced both for CLL (2.8:1) and CML (1.4:1) when compared with international data. From Pakistan Hassan et al. reported ratio of 1:1 an 4:1 for CML and CLL respectively [19]. The male predominance may partially be attributed to differential susceptibility of male sex or selective exposure to different risk factors.

Hairy cell leukaemia (HCL)

HCL represented 0.3% of all leukaemias, and 4.3% of CLL patients. It is reported to be 1-2% of all leukaemias in West[1,25]. Hassan et al. from Pakistan have reported HCL to be 0.9% of all leukaemias[19].

CML in children

CML accounted for 5.8% of all leukaemias in children upto 15 years. It is reported to be rare in children[23], and in another Pakistan study it accounted for 6.5% of all leukaemias in children and upto 12 years[24].

CONCLUSION

Chronic leukaemias are less common than acute leukaemias. In chronic leukaemias CML is significantly more common than CLL. CLL is less frequent when compared with western societies, but more frequent than African, Indian, Far Eastern and South American populations. CML on the other hand shows least geographic variation and differences rarely exceed two fold. CML appears to be more frequent in young and early middle aged adults as compared to the west where it reaches a peak between 50 and 60 years. CLL although less frequent than west, shows almost similar age related distribution.

Both the types of chronic leukaemias are more common in males. CLL however shows more pronounced male predominance.

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