Haematological Malignancies in Bahrain

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Objective: To provide an estimate of the prevalence and shift of different types of haematological malignancies over 10 years time period from 1986 to 1995.

Study Design: Relevant laboratory based data of all cases of haematological malignancies in Bahrainis diagnosed between January 1986 to December 1995. Results expressed as age specific and age adjusted incidence rates per 100,000 population per year during the periods 1986 to 1990 and 1991 to 1995.

Results: Observed prevalence of haematological malignancies increased from 3.3 in 1986 to 9.8 in 1995 per 100,000 population. In children the peak incidence was 8.7/100,000 population in less than 5 years of age. In adults the peak incidence was 40/100,000 in the 65-75 years age group. The lowest incidence of 1.8/100,000 was in the 20-30 years age group. An abrupt increase in prevalence of acute lymphatic leukaemias was observed in 1991 (post Gulf War).

Conclusion: A three times increase in prevalence rate at the end of 10 year (1986-1995) is alarming. This may be due to an increase in detection rate, though the effect of other factors such as the Gulf war cannot be completely ignored. However this study will now provide base data to observe shift in occurence over time.

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Surveillance of cancer statistics is important in public health planning and the development of strategies for its control. For this purpose the National Cancer Registry has started functioning in Bahrain only from 1994. Therefore the incidence and mortality statistics for cancers in Bahrainis is not available at the moment. The purpose of this study was to assess the occurrence of one of the cancers ie. the haematological malignancies in Bahrainis to identify shifts in occurrence over time, and to correlate the findings with other variables.

METHODS

The study was based on data relevant to 213 cases of haematological malignancies diagnosed between January 1986 to December 1995 at the Department of Pathology, Salmaniya Medical Centre, Bahrain. The diagnosis was made on bone marrow aspiration smears and bone marrow biopsies. Bone marrow aspirates were stained with Giemsa, Periodic Acid Schift (PAS), Myeloperoxidase (MPO), Sudan Black, Acid Phosphatase, non specific Esterase, Chloroacetate Esterase and Perl's stains as and when required[1]. Bone marrow biopsies were stained with haematoxylen eosin and reticulin stains. The French-American-British (FAB) classification was used for the classification of acute leukaemias and myelodysplastic syndromes[2-5].

Only Bahraini patients were included in this study. Data were examined by age, sex, age specific and age adjusted rate during reporting periods 1986-1990 and 1991-1995. Male to female ratios were calculated as age adjusted ratios. Incidence rates are reported as cases per 100,000 population per year. Throughout the text, age specific incidence rates are for the most recent reporting period (1991-1995) unless otherwise specified.

RESULTS

Trends of the Haematological Malignancies:

There were 213 cases of all types of haematological neoplastic conditions. The age adjusted male to female ratio was 1.6:1. It was almost equal (ratio 1.2) in the paediatrics age group and almost double (ratio 1.8) in the adult age group.

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Table 1. **Haematological malignancies. Frequency and percent distribution of male female ratio, median age at diagnosis and age adjusted incidence by morphology in both sexes.**

Morphology	*No*	*%*	*Male: Female ratio*	*Median age at diagnosis*	*Age adjusted rate per 100,000 population* 1986-90	1991-95
Haematological malignancies	213	100.0	1.6:1		4.4	7.9
Lymphoid leukaemias	71	33.3	1.9:1			
Acute	58	27.2	2:1	6	1.2	2.1
Chronic	13	6.1	1.6:1	66	0.3	0.4
Myeloid leukaemias	67	31.5	2.3:1			
Acute	42	19.8	1.8:1	44	0.9	1.4
Chronic	25	11.7	5.3:1	54	0.5	1.2
Myelodys plastic syndromes	25	11.7	1.2:1	58	0.7	0.7
Multiple myeloma	25	11.7	3:1	58	0.9	0.6
Primary polycythaemia	8	3.8	1.7:1	60		
Primary thrombocythaemia	5	2.3			41	
Idiopathic myelofibrosis	3	1.4				
Hypereosinophilic syndrome	4	1.9				
Chronic neutrophilic leukaemia	4	1.9				
Hairy cell leukaemia	1	0.5				

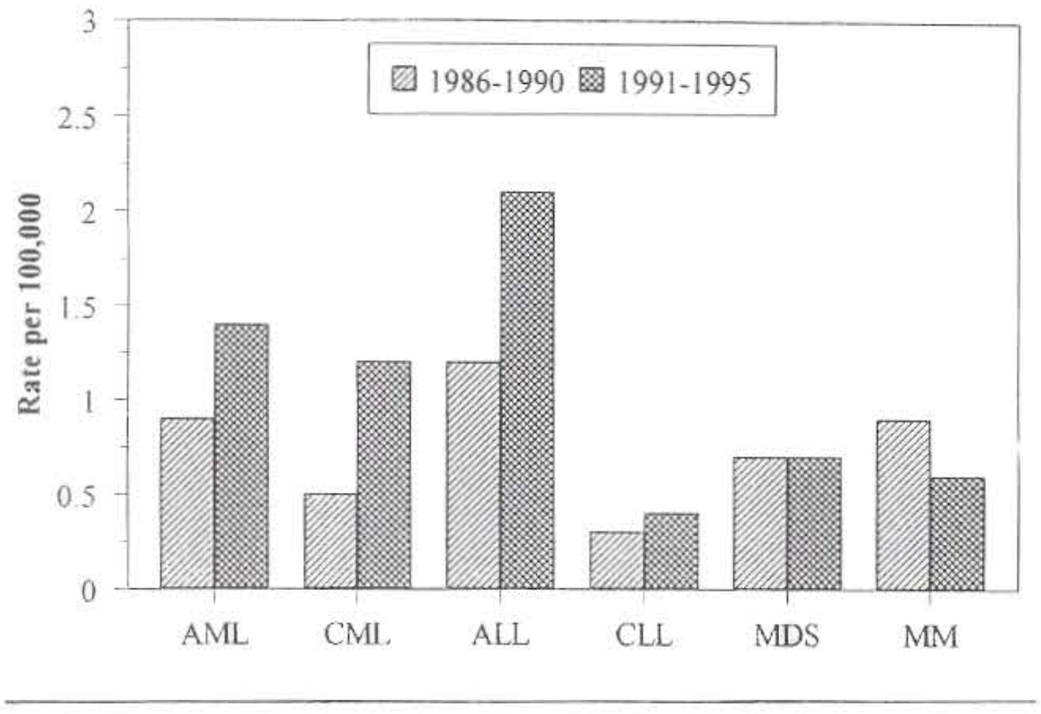

Figure 1. Haematological malignancies: Age adjusted incidence rates by histologic subtype, time period, both sexes, Bahrain.

The age adjusted incidence rate for over all haematological malignancies increased considerably during the 10 years of data collection from 3.3 in 1986 to 9.8 in 1995 per 100,000 population. This upward trend was observed mostly for some acute leukaemias and identification of more newly defined haematological malignancies (such as chronic neutrophilic leukaemia, hyper eosinophilic syndrome etc (Table 1, Figure 1). For children, the highest incidence of haematological malignancies in the most recent reporting period (1991-95) was 8.7 per 100,000 in the population younger than age 5. The rate then dropped to 3.7 in the 5-9 year age group and continued to decline to the nadir of 1.8 in the 20-30 year age group. Adults showed a progressing increase in the age specific rates, which peaked to around 40 per 100,000 for persons age 65-70 years (Figure 2).

Acute Myeloid Leukaemias (AML): There were 42 cases of acute myeloid leukaemias consistituting 19.7 % of all haematological malignancies, 21.9 % of all adult haematological malignancies and 40 % of all acute leukaemias. Male to female ratio was 1.8:1. The median age at diagnosis was 44 years. AML was found to occur as frequently as acute lymphoid leukaemia (ALL) in children less than 2 years of age, infrequent in 2-10 years age group and re-emerged in the next decade, then continued to increase till 75 years of age. The age specific rates were 1.2 per 100,000 in the 15-19 age group, 3.2 in the 35-39 age group and 6.0 in the 70-74 age group. The age adjusted incidence rate was 0.9 in 1987-90 and 1.4 in 1991-95 per 100,000. The different FAB subtypes observed were 5 (12%) cases of M_1, 9 (21.5%) of M_2, 8 (19%) of M_3, 9 (21.5%) of M_4, 8 (19%) of M_5 and 3 (7%) of M_7. No case of M_6 was observed during this period.

Chronic Myeloid Leukaemia (CML): There were 25 cases of CML constituting 11.7 % of all haematological malignancies and 37.3 % of all myeloid leukaemias. There was a distinct male predominance with a male to female ratio of 5.3:1. The median age at diagnosis was 54 years. Except

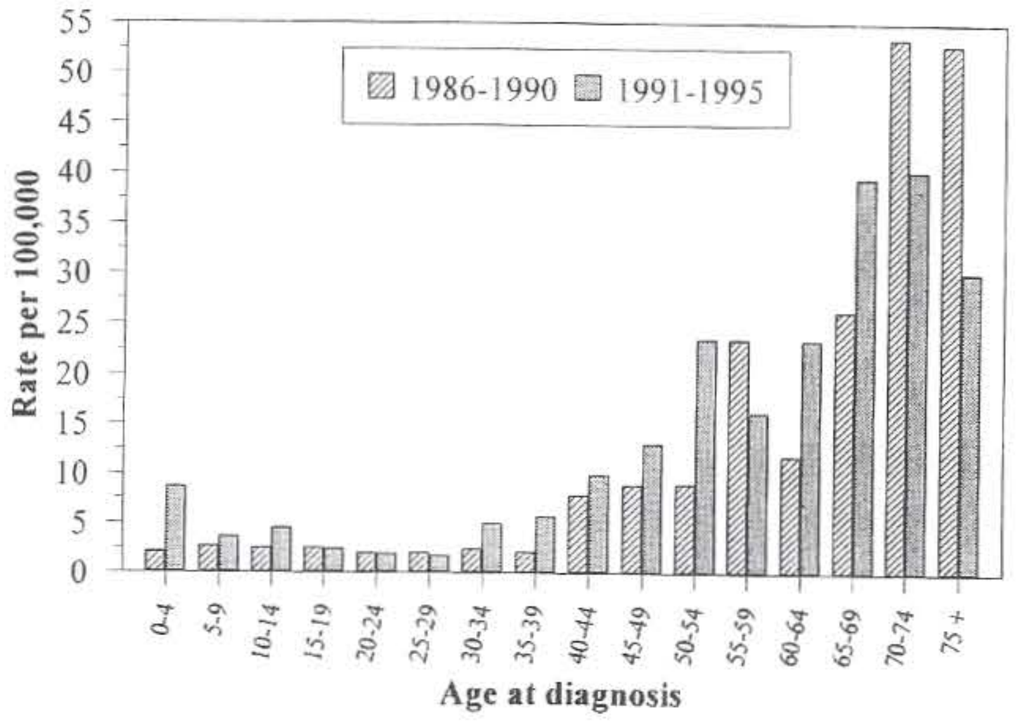

Figure 2. Haematological malignancies: Age specific incidence rates by time period, both sexes, Bahrain.

for one occasional case in a 15 year old, 80 % of the cases occurred between 30-70 years of age. The age adjusted incidence rate increased from 0.5 per 100,000 in the years 1986-90 to 1.2 per 100,000 in the years 1991-95. There were 5 (20 %) cases in accelerated phase at the time of first diagnosis. Four cases showed myeloid blastic transformation and one showed lymphoid blastic transformation.

Lymphoid Leukaemias: There were 71 cases of lymphoid leukaemia, which comprised of, acute 27.2% and chronic 6.1% and together constituted 33.3 % of all haematological malignancies. The male to female ratio was approximately 1.9:1. There was a marked difference in the age distribution of acute lymphoid leukaemia (median age 6 years) and chronic lymphoid leukaemia (median age 66 years).

Acute Lymphoid Leukaemia (ALL): There were 58 cases of acute lymphoid leukaemia constituting 27.2 % of all haematological malignancies, 81.7 % of all lymphoid malignancies and 81.0 % of all childhood haematological malignancies. The male to female ratio was 2:1 for all age groups and 1.6:1 for the paediatric age group. The age adjusted incidence rate was 1.2 per 100,000 in 1986-1990 and 2.1 in 1991-1995. This increase was due to a sharp increase in cases in 1991. The age adjusted incidence rate for this year alone was 4.6 per 100,000 population. The age specific incidence rate in children younger than age 5 was 6.7 per 100,000 in 1991-1995. The age specific rates dropped to 0.6 in the 15-20 age group and remained below 1 till 50 years of age. There was no case after this age. In the absence of immunopheno- typing only FAB classification for subgrouping was used and all 3 subgroups such as L_1, L_2 and L_3 were observed during this period.

Chronic Lymphoid Leukaemia (CLL): There were 13 cases of CLL, constituting 6.1 % of all haematological malignancies and 18.3 % of all lymphoid leukaemias. The male to female ratio was 1.6:1. The median age at diagnosis was 66 ÿears . No case was seen below the age of 40 years. The age specific incidence rate was 0.6 per 100,000 in the 40-50 age group, the rate increased to 1.4 as age advanced, then increased to 15 per 100,000 in persons older than 70 years of age. Age adjusted incidence rate was similar in both reporting periods (0.3 in 1987-90, 0.4 in 1991-95 per 100,000).

Myelodysplastic Syndromes (MDS): There were 25 cases of MDS during the study period forming 11.7 % of all haematological malignancies. There were 23 adult cases and 2 in paediatric age group. The median age was 58 years. The male to female ratio was 1.2:1. The age specific incidence rate was 0.3 per 100,000 in less than 35 years of age, increased to 1.2 in the 55 years age group then further increased to 8.3 in the next decade and 12.0 in those above 75 years of age. There were 7 (28 %) cases of refractory anaemia (RA), 6 (24 %) of refractory anaemia with ring sideroblasts (RARS), 8 (32 %) of refractory anaemia with excess blasts (RAEB), a single (4 %) case of refractory anaemia with excess blasts in transformation (RAEBt) and 3 (12 %) of chronic myelomonocyte leukaemia (CMML).

There was one case from the paediatric age group and one from the adult group who had a transformation to AML in a period of few months. The age adjusted incidence of these cases was 0.7 per 100,000 in both reporting periods.

Multiple Myeloma (MM): There were 25 cases of MM in this study period accounting for 11.7 % of all haematological malignancies. The age range was 27 to 87 years with median age of 60 years. The male to female ratio was 3:1. Only 3 cases were in less than 40 years of age. The age specific incidence was 3.6 per 100,000 in above 40 years age. Only one of the 25 cases also had plasma cell leukaemia. As this study was based on bone marrow data, cases of plasmacytoma were not included in this series. Age adjusted incidence per 100,000 was 0.9 in 1987-90 and 0.6 in 1991-95.

Other Haematological malignancies: There were 8 cases of polycythaemia, 6 cases of primary thrombocythaemia, 3 cases of idiopathic myelofibrosis, 4 cases of hypereosinophilic syndrome, one case of hairy cell leukaemia and 4 cases of chronic neutrophilic leukaemia. Besides there were 4 cases of transient myelodysplastic syndromes in newborns which did not transform to leukaemia and has not been included in this study. Except the last group all others occurred in the adults.

DISCUSSION

In the present study 213 new cases of haematological malignancies were reported among Bahrainis in a 10 years period from 1986 to 1995. During this period a large number of haematological malignancies were also documented in the expatriate populations and other Gulf country nationals residing in Bahrain. The latter cases were excluded so as to restrict the study to Bahrainis only. Since Salmaniya Medical Centre is the main referral hospital for such diseases, the statistics shown here is true for the total Bahraini population.

The data was examined by age, sex, age specific and age adjusted incidence rates during two reporting periods ie. 1986 to 1990 and 1991 to 1995. Since the incidence of specific cancer varies considerably in different age groups, comparison of crude relative frequency between countries is likely to be skewed if these countries have different population age distribution. Most accurate comparisons can only be made with age standardised data. Thus our results expressed as age specific and age adjusted incidence rates per 100,000 population per year makes it convenient and acceptible for comparisons with other studies on the basis of age, sex and race.

Two distinct age related pattern of haematological malignancies was observed; one in young children and the other in adults. In children the highest incidence of haematological malignancies in the study was in the age group below 5 years (8.7/100,000). Although the pattern is same in most races[6], the incidence in Bahrainis is slightly higher than that reported in other races (6.6 per 100,000). Among the adults the age adjusted incidence rate of haematological malignancies in blacks and white population is reported to peak at 79 per 100,000 for persons age 85 and older[6], establishing that the frequency of these disorders is much higher in older adults. Where as in the Bahraini population the peak incidence was around 40 per 100,000 in adults aged 65 to 75 after which the incidence fell to 30 per 100,000. The age adjusted male to female ratio was similar to other studies[6].

Among the different categories of haematological malignancies, acute myeloid leukaemias constituted 19.7 % of all. This is comparable to the incidence in Saudi Arabia[7] (Table 2). This is lower than that reported in some Western series where it usually comprise 40 % of all leukaemias[8]. This is most likely due to separating the MDS cases into a distinct category in our study. Some cases reported as AML with relatively low numbers of bone marrow myloblasts would now be considered MDS. There was no specific preponderance of any of the FAB subtypes of AML or MDS in our study. A significant male predominance was observed in CML cases in our study.

Table 2. **Haematological malignancies: frequencies and percent distribution by types, race both sexes and years of reporting**

Races	*White**		*Black**		*Saudi Arabia***		**Bahrain*	
Year of reporting	*(1973-87)*		*(1973-87)*		*(1983-95)*		*(1986-95)*	
	Frequency	*%*	*Frequency*	*%*	*Frequency*	*%*	*Frequency*	*%*
Total	32707	100.0	3480	100.0	553	100.0	213	100.0
Acute myeloid	7070	21.6	530	15.1	137	24.4	42	19.8
Acute lymphoid	3182	9.6	227	6.5	130	23.2	71	27.2
Chronic myeloid	3768	11.5	390	11.2	70	12.4	25	11.7
Chronic lymphoid	8967	27.3	583	16.7	38	6.7	13	6.1
Multiple myeloma	9720	30.0	1750	50.5	83	14.8	25	11.7
Myeloid plastic syndrome	—	—	—	—	23	4.1	25	11.7
Primarypolycythaemia	—	—	—	—	32	5.7	8	3.8
Idiopathic myelofibrosis		—	—	—	40	7.1	3	1.4

** Reference No 6 ** Reference No 7*

Lymphoid leukaemias constituted 33.3 % of all haematological malignancies and this is consistent with other studies[6-9] but with a different ALL to CLL ratio than that observed in the Western hemisphere. The reported ratio in white and black Americans was 1:2.6 whereas in our study it was 1:0.2 which is similar to that reported from Saudi Arabia (1:0.3)[7]. The geographic / ethnic variation in rate is greater for CLL than for any of the other leukaemia types. Highest rates are reported from America and Northern and Eastern Europe where it forms 30 % of all haematological malignancies and 70 % of all lymphoid leukaemias[8]. Lower rates were reported from South America, Caribean and exceptionally low rates from Japan, China and India[8,11-13]. Our incidence of 6.1 % of all haematological malignancies and 18.3 % of all lymphoid leukaemias is at par with that reported from Asian countries.

Acute lymphoblastic leukaemia is the predominant form of childhood leukaemia all over the world and our experience is same in Bahrain. The re-emergence of the disease in the elderly age group is observed in many populations[6,9]. This was not observed in the Bahrainis. We did not encounter any case of ALL in the elderly people during this study period. Fifty percent of our ALL cases occurred between 2-5 years of age. This is similar to those reported from Western countries and is different from Africans, where the disease is rare under 5 years of age[8,11]. The age adjusted incidence rate was 1.2 per 100,000 till 1990, then suddenly increased to 4.6 in 1991. One major happening was the Gulf War of 1990. Whether there was any contribution of this to the increased incidence of ALL can only be considered if we have similar response from other Gulf countries and specially from Kuwait.

Myelodysplastic syndromes which consist of a heterogenous group of disorders are characterised by refractory cytopenias, qualitative and quantitative abnormalities of bone marrow affecting one or more cell lines and a high progression into acute nonlymphoblastic leukaemia[4]. Since this group of disorders is a relatively recent addition to haematological malignancies, many earlier series have not listed this as a separate entity. A 11.7 % incidence in the present series confirms the importance of this condition in the epidemiological picture. This is the only situation where a marked female preponderance was observed. The median age (58 years) for this disorder was about a decade older than acute myeloid leukaemia (44 years) and slightly older than chronic myeloid leukaemia (54 years).

Myelomas encompass three categories: multiple myeloma, malignant plasmacytoma and plasma cell leukaemia. Plasmacytomas were not included in this study. Although the disease primarily affects older adults, 36 % of our patients were less than 50 years of age against 10 % reported in other series[6]. An explanation for our younger age group may be due to less number of people in the higher age groups. The rate among black population is slightly higher than in whites[6] which is higher than that observed in the Saudi Arabians and Bahrainis.

CONCLUSION

Although this is indeed a small series, we feel that we have seen some distinct and important trends in haematological malignancies in this geographical area. With newer diagnostic tools such as immunophenotyping and computerisation of data, we now hope to get better data on the epidemiology of haematological malignancies, to identify shifts in occurrence over time and to correlate these findings with other variables, such as 5 years relative survival.

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